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Vol. 31 No. 1 January, 1962

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1. Electron Microscopy of Leukocytic Margination and Emigration in Acute Inflammation in Dog Pancreas

L. R. WILLIAMSON and L. W. GRISHAM. American Jour-

J. R. WILLIAMSON and J. W. GRISHAM. American Journal of Pathology [Amer. J. Path.] 39, 239-256, Aug., 1961. 12 figs., 12 refs.

The authors, at Washington University School of Medicine, St. Louis, Missouri, have observed changes in small blood vessels which elucidate the processes involved in the localization and emigration of leucocytes in acute inflammation. In 5 dogs acute inflammation was produced by ligation of pancreatic lobules. Tissue adjacent to ligatures was removed from the side with intact circulation after intervals of 1, 2, 3, and 4 hours. Haematoxylinand eosin-stained sections showed the characteristic appearances of acute inflammation.

. Inflammatory alterations observed by electron microscopy occurred primarily in small, thin-walled vessels which lacked a muscular coat. The earliest changes were the development of intraluminal cytoplasmic processes and large intracytoplasmic vesicles (1 μ in diameter) in the endothelium. These cytoplasmic processes. were long (up to 8 μ) and thin (less than 1 μ) and, in some areas, were so numerous as to form a network in the vessel lumen. Leucocytes, predominantly ne trophils, appeared to become enmeshed in these processes and were subsequently completely enveloped by endothelial cytoplasm. When numerous leucocytes were enmeshed and enveloped in this manner, light microscopy of adjacent sections showed margination. Subsequent to margination, as the leucocyte emerged from the extraluminal margin, a new basement membrane was formed between the leucocyte and the endothelium. The new basement membrane was continuous with the original one. Concomitant with the formation of the new basement membrane the outermost membrane separating leucocytes from the extravascular space became frayed and smudged and ultimately disintegrated, releasing the leucocyte into the extravascular space. Almost all the cells emigrating were neutrophils, although occasional lymphocytes and erythrocytes were H. Caplan seen.

2. The Antihypertensive Endocrine Function of the Kidney

T. TOTH and J. BARTFAI. Clinical Science [Clin. Sci.] 20, 307-313, June, 1961. 4 figs., 15 refs.

The authors describe experiments carried out on rats at the Medical University of Budapest which provide evidence that the normal kidney has antihypertensive properties which are mediated through a hormonal mechanism. The experiments were performed on parabiotic pairs of rats, hypertension being induced in one member of the pair by the method of encasing both kidneys in slightly stretched rubber coats. This operation carried a high mortality (40 to 50%), but in the survivors was regularly followed by the development of severe hypertension within 2 or 3 days.

In the first series of experiments renal ischaemia was induced in one partner by the method described, while at the same time one kidney was removed from the other member of the pair. When this procedure was carried out immediately after the parabiotic connexion (coelic anastomosis) had been established hypertension developed only in the rat with renal ischaemia, the blood pressure of his partner remaining normal; but when the procedure was delayed for 4 days after the establishment of parabiosis the blood pressure of both animals rose together. The authors attribute this effect to the development of capillary connexions a few days after parabiosis was established which allow a pressor substance (presumably a large non-diffusible molecule) to pass from one rat to the other.

In the second series of experiments the same procedure was followed, again 4 days after parabiosis, except that nephrectomy was not carried out on the second animal. In this case neither member of the pair developed hypertension. Since the only difference between these rats and those in the first experiment was the presence of two kidneys in the second member of the pair, it appeared that the presence of two intact kidneys prevented the development of hypertension. This effect could have been the result of destruction or excretion of a pressor substance by the intact kidneys, but that this was not the case was suggested by further experiments in which the parabiotic linkage of animals with already established hypertension to normal animals with both kidneys intact was followed by a reduction in the blood pressure of the hypertensive partners within 2 days after parabiosis. Since capillary connexions could not have been established in this short period, presumably no pressor substance had reached the normal partner. The authors. suggest therefore that the intact kidneys secreted a hypotensive substance which was of small molecular size and easily diffusible and thus able to pass from one rat to the other immediately after parabiosis and lower the blood pressure of the hypertensive partner.

Lastly, when plasma from animals with intact kidneys which had shown an antihypertensive effect in the above experiments was injected intraperitoneally into single

animals with established acute or chronic renal hypertension it was shown to be effective in reducing the blood pressure of these animals, whereas injection of plasma from normal rats into hypertensive animals had no such effect.

The authors conclude that there is good evidence for the production of an antihypertensive hormone by the normal kidney.

M. Harington

CHEMICAL PATHOLOGY

3. Serum Haptoglobins: Their Semiquantitative Estimation by a Paper Electrophoretic Technique

H. C. HERMAN JR. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 57, 825-833, June, 1961. 2 figs., 21 refs.

The author describes a simple method for the estimation of haptoglobins in human serum which he has developed at Johns Hopkins University, Baltimore. It differs from those previously described in that haemoglobin C is added to the test serum instead of haemoglobin A. The principle of the method depends on the different electrophoretic mobilities of bound and unbound haemoglobin, and in performing it the amount of haemoglobin which must be added before free haemoglobin can be detected on subsequent electrophoresis, that is, before the serum haptoglobins become saturated, is determined. Haemoglobin C is preferred to haemoglobin A because of a greater difference at pH 8.6 (veronal buffer) in the electrophoretic velocities of haemoglobin A and its complex with haptoglobin. The haemoglobin from a subject with the haemoglobin-A trait (A-C) can be used if pure haemoglobin C is not available. The method is recommended for its simplicity, relative rapidity, and requirement of only inexpensive equipment. J. V. Dacie

4. Serum Haptoglobins in Hemolytic Disorders

E. C. HERMAN JR. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 57, 834-847, June, 1961. 3 figs., 29 refs.

In this paper are presented the results of the estimation, by the method described above [Abstract 3], of the haptoglobin values in normal subjects and in patients with haemolytic anaemias, haemoglobinopathies, and other, miscellaneous, disorders. Haptoglobins were markedly reduced or absent in 18 out of 23 patients with sickle-cell anaemia, but present in normal amounts in the other 5 unrelated patients. Haptoglobins were also absent in 5 out of 6 patients with hereditary spherocytosis: after splenectomy in 3 of these subjects there was an impressive rise in the haptoglobin value, unbound haptoglobin being detectable within 24 hours of the operation. A similar pattern was observed in 3 patients with pernicious anaemia after treatment with vitamin B₁₂. Here, however, haemoglobinaemia persisted for 4 to 11 days after therapy, and not until the plasma haemoglobin level fell below 4 mg. per 100 ml. did haptoglobins reappear in the serum. In patients with the sickle-cell trait the serum haptoglobin levels were slightly

below normal, but all except 2 of them showed some free haptoglobin.

The author discusses the significance of the various haem pigments which may be found in serum. Free haemoglobin, migrating on electrophoresis in the β_1 -globulin position, the haemoglobin-haptoglobin complex. and methaemalbumin are all readily separated and recognized, but this study provided no support for the concept of a haem-binding β globulin. In regard to the possibility that certain patients with haemolytic anaemia or haemoglobinopathy may have impaired ability to form haptoglobin the author points out that many such patients, although lacking the ability to bind extra haemoglobin added to their serum, nevertheless often have some haemoglobin already bound in their serum, thus showing that they do possess the ability to form haptoglobins. J. V. Dacie

5. The Laboratory Diagnosis of Macroglobulinaemia: with Special Reference to Starch-gel Electrophoresis E. A. BUTLER, F. V. FLYNN, H. HARRIS, and E. B. ROBSON. *Lancet* [Lancet] 2, 289–293, Aug. 5, 1961. 2 figs., 34 refs.

Sera from 12 patients with macroglobulinaemia, which had been confirmed by ultracentrifuge analysis, were examined at University College Hospital, London, by starch-gel electrophoresis. The abnormal protein failed to enter the starch gel when either a borate buffer or the tris-citrate-borate discontinuous buffer system (Poulik. Nature, 1957, 180, 1477) was used. When 0.02 to 0.06 M 2-mercaptoethanol was incorporated in Poulik's buffer system the abnormal protein entered the gel and formed an additional protein zone. 2-Mercaptoethanol probably breaks down the macroglobulin into subunits small enough to enter the gel. Control sera from 17 patients with multiple myeloma and other conditions associated with serum protein abnormalities did not behave in this way. Examination of serum by starch-gel electrophoresis with and without 2-mercaptoethanol is suggested as a simple clinical test for macroglobulinaemia.

J. E. Page

6. Paper Tests for Occult Blood in Faeces and Some Observations on the Fate of Swallowed Red Cells R. G. HUNTSMAN and J. LIDDELL. Journal of Clinical Pathology [J. clin. Path.] 14, 436-440, July, 1961. 11 refs.

The reliability of five paper tests for the detection of occult blood in faeces was studied at Guy's Hospifal, London. In the adult an *ortho*tolidine-sodium perborate and an *ortho*tolidine-peroxide test gave satisfactory results, although the incidence of false positive results was appreciably increased if the patient had not been kept on a meat-free diet. A guaiac test and tests with the commercially available "hematest" and "occultest" tablets were found to be unsatisfactory, giving a high proportion of false positive results, even in patients given a meat-free diet.

The authors state that false positive results with all tests were especially likely in infants and children in the absence of a meat-free diet.

M. Sandler

HAEMATOLOGY

7. Effect of Changes in Dietary Fat on Whole-blood Coagulation-time in Man

R. BUZINA, M. J. KARVONEN, P. RCINE, and O. TUR-PEINEN. Lancet [Lancet] 2, 287-289, Aug. 5, 1961. 2 figs., 26 refs.

In this investigation reported from the University of Helsinki the effect on the whole-blood coagulation time was studied in male subjects aged 35 to 64 before and approximately 6 months after a major proportion of the saturated fat in the diet of the experimental group had been replaced by largely unsaturated fats. The comparison was made between 57 and 53 patients respectively in two mental hospitals, in one of which the diet remained unchanged, while in the other it was medified by replacing whole milk by an emulsion of soyabean oil in skim milk and butter and ordinary margarine by a special brand of margarine made up mostly of unsaturated fat. These changes resulted in a decrease of saturated fatty acids and an increase of linoleic and other polyethenoid acids in the diet, the ratio of the saturated to polyethenoid acids falling from 6.6:1 to 2.0:1.

In the experimental group the change in diet resulted in a fall in the serum cholesterol level from 236 mg, to 215 mg, per 100 ml. Whole-blood coagulation time was determined by a method with a long clotting time. Before the dietary change the mean clotting time in the experimental group was 52.68 minutes, whereas 6 months later it had increased to 64.84 minutes, being shortened in only one subject in this group. There was no significant change in the control group.

A. S. Douglas

8. The Macrocytosis of Hepatic Disease: Thin, Thick and Target Macrocytosis

J. R. BINGHAM. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 178-185, July 22, 1961. 4 figs., 14 refs.

Although it has long been known that large erythrocytes (macrocytes) occur in 2 out of 3 patients with hepato-biliary disease, there has been no agreement about their frequency, origin, or significance. This paper from Toronto Western Hospital reports the results of a study of the macrocytes found in 222 patients suffering from a variety of hepatic and biliary diseases, 137 (62%) of whom were found to have a macrocytic blood picture (mean cell diameter 7-6 μ or more). Three different types of macrocyte, termed respectively thin, thick, and target macrocytes, were observed.

"Thin macrocytosis", in which the erythrocytes have the same volume as normal cells but a greater diameter and less thickness, predominated in all cases of hepatic disease in which the parenchymal cells were damaged. This condition, which was present in 81 cases, was not caused by a deficiency of any haematopoietic substance and disappeared only with the healing of the underlying hepatic disease. "Thick macrocytosis", in which the mean cell volume is raised to $110 \, \text{c.} \mu$ or more, was found in only 17 patients. It was caused by nutritional deficiency and disappeared with the administration of concentrated liver extract; it did not respond to cyanoco-

balamin therapy. Free hydrochloric acid was present in the gastric secretion in all 17 cases in this group. Target macrocytosis (10 to 50% of target cells with a mean cell diameter of $7.6\,\mu$ or more) was found in 39 patients. The presence of target cells in these cases was considered to be due to prolonged, severe biliary obstruction—a view confirmed by their disappearance when the obstruction was relieved.

A. W. H. Foxell

· MORBID ANATOMY AND CYTOLOGY

9. Toxoplasmosis in Anencephalics and the Vascular Pathogenesis of Anencephaly. (К вопросу о токооплавмовном инфекционном процессе у анэнцефалов и о дисциркуляторном генезе анэнцефалии) V. K. Велески. Журнал Невропатологии и Психиатрии [Z. Nevropat. Psihiat.] 61, 1052–1055, No. 7, 1961. 3 figs., 11 refs.

A description is given of the naked-eve and microscopic findings in an encephaly occurring in association with toxoplasmosis. Difficulties are encountered in clarifying the role of toxoplasmosis in the pathogenesis of anencephaly because the remains of the forebrain consist only of small areas of glial proliferation in connective tissue. There is complete absence of the vaultof the skull and proliferation-of the remains of the meninges. On microscopical examination of the arterioles of the meninges and neighbouring tissues the intima of these vessels is seen to contain a multitude of calcified cells uniformly basophil or containing basophil granules and projecting into the lumen. Other endothelial cells are acidophil and contain irregular or oval-shaped bodies 2 to 4μ in diameter, the intracellular form of Toxoplasma. This results in pseudocyst formation of the endothelial cell and these pseudocysts are seen projecting sharply into the lumen or even apparently free in the lumen. The pseudocysts are identical with those previously observed by the author in the lumen of the arterioles and capillaries of the brain of mental defectives suffering from postnatal toxoplasmosis.

It is thus clear that the destruction of the forebrain at an early stage of its development, before the formation of the bony vault of the skull (before the 9th or 10th week), has a vascular basis. An inflammatory process shown by the presence of lymphocytes, plasma cells, and macrophages, some with calcified inclusion bodies, goes on in the connective tissue developing in place of the forebrain until birth.

G. P. McGovern

10. A Radiographic Study of the Portal and Hepatic Venous Systems in Cirrhosis of the Liver

D. W. PIPER. American Journal of Digestive Diseases [Amer. J. dig. Dis.] 6, 499-510, June, 1961. 6 figs., 22 refs.

An x-ray study of the portal and hepatic venous systems was carried out on 6 normal and 12 cirrhotic livers obtained at necropsy at the Royal North Shore Hospital, Sydney. The injection material used consisted of bismuth oxylodide in gelatin solution. A cannula was placed in the portal venous branch to one lobe of the

liver and another in the hepatic venous branch to the opposite lobe, both cannulae being connected to a common funnel: The liver was flushed with water, then with 10% formalin. The radio-opaque solution was injected, warm, at a pressure of 30 cm. water until no further solution entered the liver. Reflux of the injection material was prevented by applying clamps when the injection was completed, and the gelatin was set by placing the liver in a refrigerator. The liver was then examined radiographically.

In all the cirrhotic livers the portal vein appeared normal, whereas in 11 of the 12 livers the hepatic vein was abnormal, sometimes grossly so, the most common abnormalities being distortion of the smaller veins and deficient filling of the hepatic venous system. The significance of the results is discussed, and it is pointed out that ascites is to be expected if the obstruction to blood flow is on the hepatic venous side of the liver, but not if the obstruction is primarily in the portal vein. The relevant literature is well reviewed.

W. H. Horner Andrews

11. Myocardial Necrosis in Subacute Bacterial Endocarditis. (Las necrosis miocardicas en la endocarditis bacteriana subaguda)

S. Franco-Browder, M. Gorodezky, and S. Aceves. Archivos del Instituto, de cardiologia de México [Arch. Inst. | Cardiol. Méx.] 31, 17-21, Jan.-Feb. [received Aug.], 1961. 4 figs., 11 refs.

Post-mortem examination at the National Institute of Cardiology of Mexico of 162 cases of subacute bacterial endocarditis revealed areas of myocardial necrosis in 44 (27%), the areas, which were usually multiple. being wider than 3 mm. in 17 cases. Rheumatic heart disease was present in 12 of these 17 patients. The mitral valve was the site of the bacterial process in 5 cases (all rheumatic), the aortic valve being the site in the other 12. Necrotic areas were recent in only 4 cases, showing that the condition is not necessarily fatal. In no case had the diagnosis of myocardial necrosis been made before death. Obstruction of a coronary artery by a septic embolus was the cause of necrosis in only one case; in all the others, the coronary arteries were patent and free from atheroma. It is concluded that the cause of the necrosis was more likely to have been biochemical M. Lubran than due to ischaemia.

12. The Effect of Estrogens on Atherosclerosis: a Postmortem Study

W. T. LONDON, S. E. ROSENBERG, J. W. DRAPER, and T. P. ALMY. Annals of Internal Medicine [Ann. intern. Med.] 55, 63-69, July, 1961. 7 figs., 12 refs.

This retrospective study was carried out at Cornell University Medical College, New York, on the aorta and coronary arteries of all (265) patients with carcinoma of the prostate gland coming to necropsy at the Bellvue group of hospitals between the years 1947 and 1957, the following procedure being adopted. Without prior knowledge of whether the patients had been treated with oestrogens or not, the degree of atherosclerosis was classified on the basis of the prosector's description

alone into 3 grades-absent or mild, moderate, and severe. The dose of oestrogen given in this series varied only slightly, ranging from 5 to 15 mg. of stilboestrol daily or equivalent doses of other oestrogens for 3 or more months. Significantly less atherosclerosis was found in the oestrogen-treated group, notably in regard to coronary lesions. The treated and untreated groups differed inasmuch as all cases with manifest metastases were given oestrogens, while some patients in the untreated group had shown no metastases at the beginning of treatment. The average level of nutrition for the untreated group, as measured by the thickness of the panniculus, did not differ from that of the treated cases irrespective of the duration of therapy. Age had no significant influence, but at least 6 to 12 months' treatment with 5 to 15 mg. of stilboestrol daily was necessary to produce a significant improvement in coronary and aortic atherosclerosis. Orchidectomy also appeared to have no influence, those treated by orchidectomy plus oestrogen therapy showing no more improvement than those given oestrogen alone.

On the assumption that the severity of the atherosclerosis before treatment with oestrogen was the same in both groups, and considering that the period of treatment was short in comparison with the patient's life span, the authors suggest that the differences observed between the treated and untreated groups must be due to actual removal of atheroma from the intima rather than to simple arrest of the atherogenesis. Thus they conclude that atheroma is a metabolically active deposit, the formation and absorption of which can be therapeutically altered, and also that since orchidectomy had no effect on the degree of atherosclerosis, the critical factor may not be the blood androgen level, but the blood oestrogen level.

[These findings confirm those of Rivin and Dimitroff (Circulation, 1954, 9, 533; Abstr. Wld Med., 1954, 16, 307) that the degree of atherosclerosis may be reversed in men treated with oestrogens for carcinoma of the prostate.]

Z. A. Leitner

13. Histochemical Studies in Atherogenesis: Human Cerebral Arteries

F. T. Zugibe and K. D. Brown. Circulation Research [Circulat. Res.] 9, 897-905, July, 1961. 19 figs., 20 refs.

Using the latest histochemical techniques, the authors have studied, at Northwestern School of Medicine, Chicago, the lipids, mucopolysaccharides, and elastic elements and the relation between them in the cerebral arteries of 75 human subjects ranging from foetuses to patients 70 years of age.

No apparent relationship could be found between lipids and mucopolysaccharides in respect of staining intensity or lipid distribution. Lipids appeared rarely in the cerebral arteries of subjects under 15 years of age. In adolescents and adults the presence of lipids was consistently observed in close association with the internal elastic membrane and with other reduplicated elastic fibres, even in the absence of severe lesions. The amount of lipid increased with age, but was not correlated with the amount of mucopolysaccharide present in any par-

ticular area. Fragmentation, fraying, and reduplication of the internal elastic membrane were not seen in foetuses, infants, and young adolescents; there was, however, an accumulation, mainly in the proximal layers of the media, of acid mucopolysaccharides hydrolysable by testicular hyaluronidase, indicating that the polysaccharide material was hyaluronic acid or chondroitin sulphate A and/or C. In contrast, in older adolescents and adults the mucopolysaccharides were resistant to hydrolysis by testicular hyaluronidase, thus agreeing with the authors' previous findings in the aorta (Circulat. Res., 1960, 8, 287); these changes, however, appeared in the cerebral arteries at a slightly later age.

Z. A. Leitner

14. Thrombi in the Hepatic Sinusoids of the Newborn and their Relation to Pulmonary Hyaline Membrane Formation

T. WADE-EVANS. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 286-292, June, 1961. 7 figs., 9 refs.

In this, the first of two papers from the University of Manchester on the subject of pulmonary hyaline membrane in the newborn, the author reports observations on the ante-mortem occurrence of thrombi in the hepatic sinusoids. For the detection of these thrombi, which are often very small, liver sections were stained by a micro-Mallory method and thrombus counts performed on groups of 50 adjacent microscopical fields, up to a maximum of 8 such groups being scanned in the largest sections. Cases with counts of 10 or more thrombi per group were classified as "positive".

Of liver sections from an unselected series of 136 infants dying in the neonatal period in 1956-7, thrombi were found in half and 27 were positive; of these 27, pulmonary hyaline membrane of "primary" type (that is, not due to inflammatory disease) was present in 20, the total number of cases of primary hyaline membrane in this series being 34. In the livers of a series of 131 stillborn infants 9 positive cases were found.

To obtain a matched control series the author studied additional material from previous years (1953-5) and was able to compare liver sections from 62 premature infants with hyaline membrane who died between 1 and 48 hours after birth with those from 60 infants without hyaline membrane who were of similar age and maturity. Of the former, 31 (50%) were "positive", as compared with only 11 (18%) of the controls, a highly significant difference. There were no significant differences between the "positive" and "negative" infants with hyaline membrane in foetal age, birth weight, degree of membrane formation, mode of delivery, or complications of pregnancy, nor between the "positive" cases in the membrane and non-membrane groups. In 52 instances pairs of blocks from the right and left lobes of the liver were compared, but again no differences were observed. In 40 positive cases sections from other organs showed only occasional thrombi. Lastly, liver sections from 246 adults coming to necropsy were similarly studied. In these cases thrombi were seen only in circumstances in which there had been circulatory disturbances in the liver. Discussing the possible mechanisms of thrombus formation, the author suggests that they arise in situ as a result of circulatory impairment, a conclusion which supports the view that circulatory factors are important in the genesis of primary hyaline membranes.

E. G. Hall

15. Pulmonary Hyaline Membranes, Aspiration and Pneumonia

T. WADE-EVANS. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 293-301, June, 1961. 10 figs., 10 refs.

In this second paper [see Abstract 14] the author draws attention to a current tendency to regard the formation of hyaline membrane as a specific disease process and presents material to emphasize the importance of distinguishing membranes due to inflammatory causes from "primary" membranes:

The cases reviewed included 727 infants dying in the first week of life during the years 1949-58. Membranes were found in 175 instances, of which 32 were considered to be due to pneumonia. Membrane formation was seen in 6 out of the 25 cases showing evidence of gross aspiration of vernix, meconium, or mucus; only in these 6 was there evidence of pneumonia. Among the features distinguishing the 6 from cases of "primary" hyaline membrane were: (1) the infants were all mature; (2) meconium contamination of the respiratory tract was frequent; (3) the lungs showed an alternating pattern of aeration and non-aeration; and (4) the membranes were patchy, occurred only in relation to inflammatory exudate, and differed histologically from "primary" membranes. It is considered likely that infection had occurred at the time of aspiration. In 18 cases membranes were found in association with diffuse pneumonia, the latter being considered to have most frequently originated shortly before or during delivery. The membranes in these cases were frequently similar to "primary" membranes; the author discusses the differentiation of the two types and the difficulty of distinguishing between "primary" membrane formation with added pneumonia and primary pheumonia resulting in membrane formation. In a further 8 instances membranes were seen in conjunction with inflammation which was thought to have been acquired after birth.

Summing up, the author suggests that particular attention should be paid to the possibility of a pneumonic origin before diagnosing "primary" hyaline membrane disease in mature infants or when death occurs within a few hours or is delayed much beyond 2 days after birth. He emphasizes the importance of excluding such cases when attempting to study the pathogenesis of primary hyaline membrane disease.

E. G. Hall

Needle Biopsy of the Pleura in the Diagnosis of Pleural Effusion: a Report of 118 Cases

F. HAMPSON and A. J. KARLISH. Quarterly Journal of Medicine [Quart. J. Med.] 30, 249-255, July, 1961. 6 figs., 14 refs.

This paper from the Royal Berkshire Hospital and the Central Chest Clinic, Reading, deals with a study of 136 needle biopsies of the pleura from 118 patients of widely differing ages. The material was examined by conven-

tional histological techniques. The positive specific diagnoses made in these cases, in all of which there was pleural effusion, were tuberculosis and malignant disease. The authors wisely point out that this technique, although useful in itself, should be combined with other diagnostic procedures. This is well illustrated by the fact that of the tuberculous cases, only 75% were diagnosed correctly by needle biopsy of the pleura alone, while this figure rose to 94% when other methods such as examination of sputum and gastric washings were performed in addition. Similarly encouraging results, though with lower figures, were obtained in cases of malignant disease.

G. J. Cunningham

17. Changes in the Bronchial Epithelium in Primary Lung Cancer

R. CARROLL. British Journal of Cancer [Brit. J. Cancer] 15, 215-219, June [received Aug.], 1961. 4 figs., 21 refs.

The relationship of squamous metaplasia, basal-cell hyperplasia, and intra-epithelial carcinoma of the bronchial epithelium to invasive primary lung carcinoma was studied in 92 primary lung tumours resected at Hammersmith Hospital, London, between 1952 and 1958. In every tumour examined the bronchial epithelium adjacent to the tumour was present and in many instances bronchial epithelium at some distance from the tumour was also present. The tumours were classified as squamous carcinoma in 53 (58%) of the cases, as oat-celled carcinomata in 14 (15%), and as adenocarcinomata in 11 (12%). A number of observers could not reach complete agreement concerning the histology in 14 cases; these formed an unclassified group, largely showing no tendency to differentiation.

A high incidence of basal-cell hyperplasia was found in the squamous, oat-celled, and unclassified groups, but basal-cell hyperplasia was not observed in any of the cases of adenocarcinoma. The most extensive changes were found in the bronchial epithelium of cases of squamous carcinoma.

The relevant literature is discussed. The author concludes that a large number of primary carcinomata of the lung arise from the basal cells of the bronchial epithelium and that the malignant cells may exhibit one or more lines of cytological differentiation or show no such tendency. The association of squamous carcinoma and squamous metaplasia is regarded as coincidental.

A. W. H. Foxell

18. Post-mortem Radiography and Gaseous Fixation of the Lung

R. J. R. Cureton and D. H. Trappell. *Thorax* [*Thorax*] 16, 138–143, June, 1961. 4 figs., 9 refs.

The authors of this paper from St. Bartholomew's Hospital, London, describe a technique for inflation and fixation of whole lungs with formaldehyde gas. The apparatus is simple and fixation occurs within 3 days. Once this procedure is accomplished excellent radiographs of the whole lung or of lung slices can be obtained with a portable x-ray apparatus. This technique is chiefly important because for the first time it permits good correlation between the radiological and histological appearances.

G. J. Cunningham

19. Biopsy Diagnosis of Periarteritis Nodosa: Glomerulonephritis and Renal Arteriolitis as Aids

V. J. PATALANO and S. C. SOMMERS. Archives of Pathology [Arch. Path.] 72, 1-7, July, 1961. 5 figs., 16 refs.

This is a report from Boston University School of Medicine on the pathology of 30 cases with a postmortem diagnosis of periarteritis nodosa. The average age at death was 45. No drug reactions were recorded in these cases. Some degree of hypertension was present in 12 cases at some time during their stay in hospital; only 6 cases showed eosinophilia. The most common sites of vascular lesions were the kidney, liver, heart, adrenal glands, gastro-intestinal tract, pancreas, and spleen, in that order. Microscopically, polymorphonuclear leucocytes predominated in the vessel walls and periarterially. Usually all layers of affected vessels were involved, but occasionally only the intima or adventitia showed necrosis. Thrombosis, periarterial fibrosis, recanalization, and perivascular haemorrhage were observed. Sections of kidneys showed arteritis or arteriolitis in 21 of the 30 cases; glomerular lesions were present in all 30 cases, the lesions being of several different varieties. In view of this frequent post-mortem finding of renal involvement the authors recommend diagnostic renal biopsy.

In the present series diagnosis was made on skin biopsy in one case and on cholecystectomy specimens in 2; arteriolitis was seen in one kidney biopsy. It is stated that only 4 of 31 necropsy sections of muscle showed vascular lesions.

[The title of this paper is misleading; it is not primarily a biopsy study.]

G. Loewl

20. Shearing of Nerve Fibres as a Cause of Brain Damage Due to Head Injury: a Pathological Study of Twenty Cases

S. J. Strich. *Lancet* [*Lancet*] **2**, 443-448, Aug. 26, 1961. 13 figs., 21 refs.

It is pointed out that although head injury is the most common cause of neurological disorders in Great Britain, remarkably little is known about the pathology of brain damage in this condition. There are various reasons for this. Only a few brains from patients with acute head injuries or post-traumatic neurological signs are seen by neuropathologists (and when they are they are often difficult to study because they have been so mishandled). "Because it is tedious to examine a brain histologically, pathologists have been content to study the damage visible to the naked eye—such as lacerations or coup and contre-coup lesions—which are often not the cause of the patient's death or even of his neurological signs".

The author of this paper from the Maudsley Hospital, London, discusses not lacerations or contusions, but the fact that "fibres as delicate as those of which the organ of mind is composed are liable to break as a result of violence to the head". His observations provide evidence that the extensive white-matter lesions, both of hemisphere and brain stem, represent a secondary degeneration of nerve fibres which have been stretched or torn by the shearing stresses or strains set up during

rotational acceleration of the head at the time of injury. This degeneration may follow a closed and apparently uncomplicated head injury, leaving the patient permanently incapacitated and more or less demented. The pathological findings in 20 patients surviving 2 days to 2 years after head injury are used to illustrate the condition. The author states that no estimate of the real incidence of this shearing of nerve fibres can be given as the cases were highly selected and not enough acute cases have been examined. "Only severe examples of the condition are reported here, but there is every reason to suppose that lesser degrees occur in patients with trauma to the head whether the skull is fractured or not. It also seems possible that if nerve fibres are stretched rather than torn, the lesions may be reversible at some stage, and may play a part in the production of the signs of concussion."

[This paper is important and of interest to all clinicians interested in head injury.] J. MacD. Holmes

21. Diabetic Retinopathy

J. R. Wolter. American Journal of Ophthalmology [Amer. J. Ophthal.] 51, 1123-1141, May, 1961. 35 figs., 29 refs.

Recent advances in knowledge of the histology of diabetic retinopathy encourage the hope that the continued application of special methods to the study of this condition will lead to the discovery of its cause. The present paper from Wayne County General Hospital, Eloise, Michigan, is based on the post-mortem findings in the eyes of 8 diabetic patients, the retinal changes being studied by the silver-carbonate methods of Hortega.

The changes observed were as follows: vascular damage, the proliferation of vascular (antidromic) nerves, the degeneration of neurones, the phagocytic activity of retinal microglia, the deposition of fat and hyaline, the retinal gliosis, the formation of drüsen of the pigment epithelium, and punctate and diffuse retinal and preretinal haemorrhages.

A. Lister

IMMUNOPATHOLOGY

22. Precipitating Autoantibodies in Sjögren's Disease J. R. Anderson, K. G. Gray, J. S. Beck, and W. F. Kinnear. *Lancet* [*Lancet*] 2, 456–460, Aug. 26, 1961. 3 figs., 33 refs.

The authors, working at the University, the Western Infirmary, and the Ophthalmic Institution, Glasgow, have used a variety of immunological methods in a search for precipitating antibodies in the sera from 29 cases of Sjögren's disease. In gel-diffusion plates 9 sera gave well-marked lines of white precipitate (sometimes double or treble) when allowed to react against saline extracts of various normal tissues, human thyroid gland being finally the tissue most often used after trial of a variety of tissues. Other methods successfully used to detect these antibodies included complement fixation and immunoelectrophoresis.

At least two antigen-antibody systems could be distinguished, some sera containing one antibody and others both antibodies. Both antigens were cell constituents, one being probably a protein, and they were present in various human tissues (thyroid, salivary, and lacrimal glands, spleen, and leukaemic leucocytes among others) as well as in tissues from laboratory animals. In one patient with rheumatoid arthritis (not included in this series) the serum contained both antibodies in low titre and the tissues examined post mortem were found to contain both antigens. The antibodies were thus true autoantibodies and not isoantibodies. Although some of the sera contained large amounts of antibody, the authors do not consider that they were of pathogenic significance since neither their presence nor the titre could be correlated with the patient's clinical state.

Fluorescent-antibody studies showed that the sera also contained antibodies which were able to combine with cytoplasm or nuclei of normal tissues, but the relation of these to the two autoantibodies described above was uncertain. In addition an increased incidence of anti-thyroglobulin antibody was found; thus 10 out of 24 sera tested agglutinated erythrocytes coated with thyroglobulin, 4 of them to a titre of more than 1:1,000. In similar tests on the sera from 150 patients not suffering from collagen diseases which were examined as controls only 2 gave marked precipitin lines in gels. One of these patients had received repeated blood transfusions and the other was later found to have Mikulicz's disease.

[This paper contains much experimental detail that cannot adequately be summarized and is well worth reading in full.]

M. C. Berenbaum

23. Study of Complement-fixing Structures in Aschoff's Nodes in Auricular Appendages Removed at Operation. (Nachweis komplementbindender Strukturen in Aschoffschen Knötchen operativ entfernter Herzohren)

K. KUPPER, E. LANGER, and P. KLEIN. Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin [Virchows Arch. path. Anat.] 334, 342–350, 1961. 3 figs., 29 refs.

At the Medical Academy, Düsseldorf, the authors have studied the distribution of material capable of combining with guinea-pig complement in the hearts of 48 patients with mitral stenosis and 12 with congenital heart disease as controls. Frozen sections of the auricular appendix removed at operation were treated with guinea-pig complement, the site of uptake of complement being then stained with fluorescein-conjugated antibody to guinea-pig complement. Decomplemented guinea-pig serum served as control. In all 27 mitral patients with rheumatic heart disease the Aschoff nodes were always stained and the lining of the endocardium in most cases, while the endothelial lining of the coronary arteries and the subendocardial connective tissue were sometimes stained. In 6 of the 12 control hearts staining of the lining cells of the endocardium was noted. The authors suggest that the sites of fixation of complement represent the location of antigen-antibody complexes, which in the patients with mitral stenosis were related to the disease and in the control patients to subclinical infections. G. L. Asherson

Microbiology and Parasitology

24, MethicIllin-resistant Staphylococci

M. BARBER. Journal of Clinical Pathology [J. clin. Path.] 14, 385–393, July, 1961. 5 figs., 13 refs.

This article from the Postgraduate Medical School of London describes the effect on 9 penicillin-sensitive and 9 penicillin-destroying strains of Staphylococcus pyogenes of passage 45 to 50 times on increasing concentrations of methicillin.

At the beginning of the investigation all strains were inhibited by 1.5 to 3 μg . of methicillin per ml., but after passage the minimum inhibitory concentration was 100 μg . per ml. or more for 9 strains and only 12 μg . per ml. for 3 strains, while the remainder showed intermediate degrees of resistance. Penicillinase-producing cultures became resistant more quickly than penicillinsensitive strains. Resistance was due to drug tolerance and not to destruction of methicillin. Although all strains were initially inhibited by 0.06 unit of benzylpenicillin per ml., they showed considerable degrees of resistance to benzylpenicillin after passage on the methicillin plates, although those which became most resistant to one did not necessarily show the greatest resistance to the other.

All 13 strains resistant to $25 \mu g$. of methicillin per ml. were compared with their parent strains. Cultures derived from penicillin-sensitive strains (6) multiplied less rapidly, showed variation in colonial size, and quickly reverted to the sensitive state if subcultured in the absence of methicillin. The cultures derived from penicillin-destroying strains, with one exception, had characteristics similar to those of the parent strains and retained their resistance in the absence of methicillin (12 passages). In all cases phage sensitivity was unaltered.

Naturally occurring methicillin-resistant strains of Staph. pyogenes were found to be uncommon, only one being found in 500 infective strains in the hospital and only one in over 4,000 strains at the Central Public Health Laboratory.

A. E. Wright

25. Erythromycin-resistant Staphylococcus aureus
A. F. MACCABE, J. C. GOULD, and J. O. FORFAR. Lancet
[Lancet] 2, 7-9, July 1, 1961. 1 fig., 14 refs.

Over a period of 2 years (July, 1958, to August, 1960) the incidence of infection by strains of Staphylococcus aureus resistant to 2 μ g. of erythromycin per ml. was investigated in a large general hospital in Edinburgh. During the first year such strains were comparatively infrequent, but in March, 1960, no fewer than 22 out of 96 strains were found to be resistant. Although the majority of erythromycin-resistant strains came from the paediatric and maternity departments, such organisms eventually spread to other departments as well. Since no less than 91% of the resistant strains belonged to one phage type (75/76/77) the suggestion is made that it is only certain strains that can become resistant to

erythromycin; but that if this antibiotic is employed at all extensively the survival and dissemination of such strains are encouraged.

R. Hare

26. Immunofluorescence in Diagnostic Bacteriology. III. The Identification of Enteropathogenic *E. coll* Serotypes in Fecal Smears

F. COHEN, R. H. PAGE, and C. S. STULBERG. American Journal of Diseases of Children [Amer. J. Dis. Child.] 102, 82-90, July, 1961. 1 fig., 11 refs.

Ordinary bacteriological and serological techniques for the identification of pathogenic coliforms take at least 48 hours. It would therefore be a great advantage to have a technique utilizing a fluorescent antibody, thus allowing a diagnosis to be made immediately on a wet preparation. In this investigation reported from the Child Research Center and Children's Hospital of Michigan, Detroit, fluorescent antibodies were prepared against 9 specific types of Escherichia coli. The antisera were carefully titred and their capability of fluorescent staining estimated. Two polyvalent pooled sera were prepared with appropriate dilutions so that each individual serum was acting at its best strength. Faeces which had been submitted to the laboratory for normal bacteriological diagnosis were stored at -20° C. for future reference. These were later thawed and smears made with the two polyvalent fluorescent antibodies and also with the appropriate specific sera. Broth cultures of each thawed specimen were also prepared and smears from these cultures were similarly examined after incubation for 4 and 20 hours. In 35 out of 87 stool specimens studied the identification of fluorescent organisms in the faecal smears corresponded with the original bacteriological identification. Of these 35 specimens, only 16 grew when they were recultured in broth, but all these were identified by the specific fluorescent antibody as well as bacteriologically and the results corresponded exactly with those observed in the faecal smears in the original cultures. With 6 specimens fluorescent staining of smears was negative, but staining of the broth cultures was positive, illustrating the value of examining both direct smears and smears from cultures. In 6 instances the faecal smears or broth cultures were positive in spite of the original bacteriological tests being negative. In 5 specimens the fluorescent staining methods gave negative results whereas the original culture was positive. In 35 specimens the results were negative by all tests.

The authors showed that the fluorescent staining technique was very accurate when performed under proper conditions, but they emphasize that the reliability of the fluorescent antibody procedure depends greatly upon the preparation and testing of the antigenic sera, careful attention to the standardization of these sera, and their use at their optimum strength.

R. F. Jennison

Pharmacology and Therapeutics

- 27. Clinical and Metabolic Studies on a New Anabolic Steroid, "Oxymetholone"
- R. M. MYERSON. American Journal of the Medical Sciences [Amer. J. med. Sci.] 241, 732-738, June, 1961. 1 fig., 15 refs.

The clinical effects of a new synthetic steroid, "oxymetholone", in chronic malnutrition were studied in 31 patients at the Veterans Administration Hospital, Philadelphia. The drug was given in a dosage of '7.5' mg. daily for at least 3 weeks. It was found that 21 of the patients gained 5 lb. (2.26 kg.) or more in weight, the average gain being 8.1 lb. (3.6 kg.). The greatest gain occurred in the first week, but there was no fixed pattern of weight change. In patients who failed to gain or who had ceased to gain weight doubling the dosage of the drug had no effect. Some of the patients experienced a feeling of well-being and an improvement in appetite. Water retention and side-effects (other than soreness of the tongue in one case) were not observed. Growth of any tumour present was not stimulated. Balance studies in 2 cases showed that although nitrogen retention occurred, this was not increased when the dosage of the drug was trebled.

The steroid was without beneficial effect on 3 patients with severe emphysema.

A. Gordon Beckett

28. The Effect of Atropine, Propantheline and Poldine on the Vagally Stimulated Gastric Motility and the Histamine-stimulated Acid Gastric Secretion in the Rat

P. N. AARSEN and J. VAN NOORDWUK. British Journal of Pharmacology and Chemotherapy [Brit. J. Pharmacol.] 17, 41–50, Aug., 1961. 5 figs., 15 ress.

The effect on histamine-stimulated acid gastric secretion in rats of doses of atropine and atropine-like drugs which reduce or abolish stomach motility has been studied experimentally at the Pharmacotherapeutic Laboratory, University of Amsterdam, the required doses being determined by recording the effect of the drugs on gastric contractions induced by vagal stimulation.

Histamine-induced acid gastric secretion in anaesthetized rats was not diminished by intravenous poldine methylmethosulphate in a dose (2 μ g.) that reduced vagally stimulated gastric contractions by approximately 75%. An intravenous dose of atropine sulphate (11·2 μ g.) twice as large as that which normally reduced gastric contractions by 75% had no apparent effect on histamine-stimulated acid gastric secretion up to 2 hours after injection; a dose of 500 μ g. of atropine sulphate, however, caused a slight inhibition of acid secretion in 80 to 120 minutes. Propantheline bromide in a dose (5·2 μ g.) that inhibited gastric contractions by approximately 75% slightly diminished acid secretion in 40 to 80 minutes; this effect was not increased by a second injection (10·4 μ g.) of propantheline. It is concluded that any

inhibition of acid gastric secretion that occurred was an indirect effect, possibly caused by interference with blood flow through the stomach wall, and could not be attributed to anti-muscarine or direct toxic effect.

J. E. Page

29. Excitomotor Effect of Serotonin (5-Hydfoxytryptamine) on the Small Intestine in Man. Radlographic Study. (Effet excito-moteur de la sérotonine (5-hydroxytryptamine) sur l'intestin grêle humain. Étude radiographique)

C. Debray, F. Besançon, R. Buchet, and J. Émerit. Archives des maladies de l'appareil digestif et des maladies de la nutrition [Arch. Mal. Appar. dig.] 50, 721-728, July-Aug., 1961. 4 figs., 5 refs.

The authors have studied radiologically the effect of serotonin (5-hydroxytryptamine) on the motility of the small intestine in 5 normal subjects and 2 gastrectomized patients at the Hôpital Bichat, Paris. When the jejunum or ileum was seen to be well filled with barium 1 mg. of serotonin was given intravenously and serial radiographs taken during the following 10 minutes. Vigorous contractions of the duòdenum and proximal jejunum were seen within one minute of the injection, and these spread distally during the next few minutes. There was little if any effect on ileal motility, but the duodenal and jejunal contents were evacuated into distal segments within 5 minutes of the injection of serotonin. The jejunal mucosal pattern was accentuated, probably as a result of contraction of the longitudinal muscle.

P. C. Reynell

30. Serotonin (5-Hydroxytryptamine) and the Physiological Motility of the Small Intestine in Man. Electromanometric Studies. (Sérotonine (5-hydroxytryptamine) et motricité physiologique de l'intestin grêlè humain. Recherches électromanométriques)

C. Debray and F. Besançon. Archives des maladies de l'appareil digestif et des maladies de la nutrition [Arch. Mal. Appar. dig.] 50, 729-735, July-Aug., 1961. 8 refs.

In this further study [see Abstract 29] the gastrointestinal tract of 11 male subjects was intubated for a part or the whole of its length with polyvinyl catheter's filled with water and having lateral orifices spaced at distances of 20 cm. to one metre through which pressure changes were recorded electromanometrically. A single intravenous injection of 0.5 mg. of serotonin produced strong contractions of the duodenum and jejunum, but little response in the ileum or colon. The intestine was relatively refractory to a second injection given a few minutes later. The contractions were similar to those sometimes recorded spontaneously, and it is suggested that the response to serotonin represents an exaggerated form of a physiological phenomenon, so that serotonin may be a chemical transmitter responsible for normal-P. C. Reynell duodenal and jejunal contractions.

9

31. Systemic and Coronary Hemodynamic Effects of Erythrol Tetranitrate

G. G. Rowe, C. J. Chelius, S. Afonso, H. P. Gurtner, and C. W. Crumpton. *Journal of Clinical Investigation* [J. clin. Invest.] 40, 1217–1222, July, 1961. 9 refs.

The results of experiments on animals have indicated that an increase in coronary blood flow follows the intracoronary administration of nitrates. Observations in man, however, suggest that the relief of angina pectoris may be through a reduction in cardiac work rather than through any specific effect on the coronary circulation itself. The present paper reports from the University of Wisconsin a study of the effects of erythrol tetranitrate on 15 subjects, of whom 7 had a normal cardiovascular system, 4 had arterial hypertension but no angina pectoris, and 5 had been admitted to hospital because of angina pectoris. Two cardiac catheters were used, one lying in the pulmonary artery and the other in the coronary sinus. A needle tip was placed in the femoral artery, cardiac output being determined by the Fick principle and coronary blood flow by the nitrous oxice saturation method.

In 9 cases, including 5 of the normal subjects and the 4 patients with hypertension, the sublingual administration of 7.5 to 15 mg. of erythrol tetranitrate produced no untoward changes in the blood pressure, pulse, and respiration. In 3 cases, however, including one normal subject and 2 of the patients with angina pectoris, there was marked hypotension, with a slowing of the heart rate and development of a shock-like state. (The data for the 7th normal subject were incomplete.) The detailed results are tabulated and demonstrate a fall in cardiac output with decrease in the work of the heart. The coronary blood flow was not altered, but the coronary vascular resistance decreased by a mean of 15%; the myocardial oxygen consumption was not changed. It is therefore concluded that the effectiveness of nitrates would seem to be due to their ability to reduce cardiac work to a level commensurate with an attainable coronary blood flow.

32. The Effect of Persantin on Coronary Flow and Cardiac Dynamics

E. C. Elliot. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 469-476, Aug. 26, 1961. 7 figs., 73 refs.

In the dog 95% of the coronary venous return enters the right side of the heart via the coronary sinus and the anterior cardiac veins. This allows it to be separated from the rest of the venous return and so permits its accurate measurement by direct means. This fact was utilized in the studies here reported from the University of Alberta, Edmonton. In each of 10 anaesthetized dogs the whole of the venous return, including that from the coronary circulation, was collected into a venous reservoir from whence it was pumped at a constant rate into the pulmonary artery. By maintaining a constant rate of pumping throughout the experiment the cardiac output could be maintained at a constant rate.

About 15 or 20 minutes were allowed for the preparation to stabilize before measurements of the blood pres-

sure, heart rate, coronary flow, and myocardial oxygen consumption were made. When the coronary dilator drug "persantin" (RA8, one of the compounds with a pyrimido-pyrimidine system) was injected into the pulmonary artery in a dosage of 0.3 mg, per kg, body weight the blood pressure fell, the coronary flow rose, the arteriovenous oxygen difference decreased, but the heart rate was not significantly affected. The maximum increase in coronary flow occurred about 3 minutes after the injection of the drug and the main effect lasted 9 to 15 minutes. When the blood pressure was below 100 mm. Hg persantin produced a smaller increase in coronary flow, but the effect was more prolonged. Since the increase in coronary blood flow occurred while the cardiac output was constant, the arterial blood pressure reduced, and the heart rate slightly showed, it is suggested that persantin must have decreased the peripheral resistance in the coronary vessels to a marked degree.

P. A. Nasmyth

33. Study of the Mechanism of Action of Hydrochlorothiazide in Arterial Hypertension. The Role of Hypokalaemia. (Étude du mécanisme d'action de l'hydrochlorothiazide dans l'hypertension artérielle. Rôle de l'hypokaliémie)

D. FRITEL, J. QUICHAUD, M. HODARA, and J. TRUFFERT. Revue française d'études cliniques et biologiques [Rev. franç. Ét. clin. biol.] 6, 560-573, June-July, 1961. 50 refs.

At the Hôpital Beaujon-Clichy, Paris, the authors have investigated the mechanism of action of hydrochlorothiazide in 10 men and 6 women whose average age was 47 years and all of whom had relatively severe hypertension of over 2 years' duration; 9 had changes in the fundus of the eye, but none showed any signs of cardiac failure or renal insufficiency. All forms of hypotensive treatment were stopped at least 8 days before carrying out the experiments, in which hydrochlorothiazide was given in a dosage of 50 mg. twice daily. In 12 of the 16 subjects there was a fall of 10% or more in the arterial blood pressure, both systolic and diastolic, with an average of 14% on the 10th day, while after 15 days the pressure was still reduced. Of the 12 subjects who thus responded, 4 were receiving a low-salt diet and in these the systolic pressure had fallen by 17% and the diastolic by 23% by the 10th day. Measurement of the plasma volume in 4 patients with a normal intake of salt, including one who was resistant to the action of hydrochlorothiazide, showed that this value was reduced by 13 to 18%.

It was demonstrated that the fall in blood pressure was largely related to a reduction in the concentration of potassium in the plasma, but not that in the cells, and that such reduction was greater when the sodium intake was restricted. Thus the hypotensive effect of the drug was abolished or greatly lessened when 3 or 4 g. of potassium was added to the diet, while the intravenous administration of insulin and glucose (which causes a lowering of the plasma potassium concentration) increased the effectiveness of hydrochlorothiazide unless potassium citrate was given at the same time. It would therefore appear that the action of hydrochlorothiazide in lowering

blood pressure is largely related to its effect on the concentration of potassium in the plasma.

W. H. Horner Andrews

34. Haemodynamic Effects of Guanethidine

C. T. Dollery, D. Emslie-Smith, and J. P. Shilling-ford. *Lancet* [*Lancet*] 2, 331-334, Aug. 12, 1961. 3 figs., 11 refs.

Haemodynamic studies were made at the Postgraduate Medical School (Hammersmith Hospital), London, on 13 severely hypertensive patients receiving treatment with guanethidine. Serial estimations of change in cardiac output were made by a dye-dilution method in which equal doses of Coomassie blue were injected into the right atrium at intervals. Dye curves were recorded from an ear oximeter and calibration was such that changes in cardiac output could be estimated by comparison of the reciprocals of the areas enclosed by the curves when plotted semilogarithmically.

Tilting with the feet down reduced the blood pressure in 7 out of 11 patients, with a corresponding fall in cardiac output of 4% to 54% (mean 24%). Of 12 patients exercised by pedalling a bicycle ergometer in the horizontal position, in 8 there was a fall in blood pressure with, in 7 of them, a rise in cardiac output of 33 to 215% (mean 102%). In 5 patients in whom the rebound phase was studied after cessation of exercise the blood pressure rose to its previous level or higher, while in 4 of them the cardiac output was still above the resting level. Intravenous injection of guanethidine in 5 cases (in 3 as the first therapeutic dose) was followed by a rise in blood pressure, but no significant change in cardiac output.

K. G. Lowe

35. Clinical Investigations on a New Intramuscular Haematinic

N. S. E. Andersson. British Medical Journal [Brit. med. J.] 2, 275-279, July 29, 1961. 5 figs., 14 refs.

Clinical studies of a new haematinic for intramuscular use—"jectofer", an iron-sorbitol-citric-acid complex with dextrin as a stabilizer—are reported from Central-lasarettet, Danderyd, Sweden. The solution contains 50 mg. Fe per ml. and has a pH of 7.5. When a dose is injected into a rabbit two-thirds is absorbed within 3 hours and 80 to 85% after 12 hours; about 30% of the iron is excreted in the urine. The L.D.50 for mice is about 35 mg. per kg. body weight. A series of 65 patients "who satisfied the clinical criteria for stabilized iron deficiency" took part in the trial. Of these, 34 were treated with the iron-sorbitol preparation in a dose of 100 mg. Fe daily and 31 were given iron-dextran ("imferon") and the results compared.

After 5 weeks the haemoglobin level had risen by 3.8 g. per 100 ml. in patients given iron-sorbitol and by 3.9 g. per 100 ml. in those given iron-dextran. No general reactions were reported in the patients treated with iron-sorbitol, though some of them noticed that one hour after the injection the sense of taste was affected; this reaction had disappeared after about 12 hours. In 5 cases treated with iron-sorbitol a mild local reaction at the site of injection was noticed. One patient treated

with iron-dextran had a mild pyrexia and a further 6 complained of pain at the site of injection. Because of the high excretion of iron in the urine of patients treated with iron-sorbitol the renal function of 10 of these patients was investigated, but no evidence of renal damage was found.

The increases in haemoglobin value suggest that 60% of the iron injected was utilized, and as approximately 30% is excreted in the urine this means that at least 90% was absorbed from the site of injection. In the case of iron-dextran the utilization is about the same, but very little is excreted in the urine and this suggests that an appreciable quantity of iron may remain in the muscle. No discoloration of the skin was noted in either group, presumably because only 100 mg. of iron contained in 2 ml. of solution was used. It is concluded that iron-sorbitol gives very similar results to those obtained with iron-dextran.

The author claims that no sarcomatous lesions have developed in animal experiments with iron-sorbitol. The L-D.50 of 35 mg. per kg. is very much lower than that of other parenteral iron preparations; nevertheless the author considers that the margin between the clinical dose and the toxic dose is adequate.

R. F. Jennison

36. A Guide to Anticoagulant Therapy

B. ALEXANDER and S. WESSLER. Circulation [Circulation] 24, 123-138, July, 1961. 1 fig., 15 refs.

37. Diuretic Response to Chlorthalidone

A. DOUGLAS, R. HALL, D. B. HORN, D. N. S. KERR, D. T. PEARSON, and H. RICHARDSON. *British Medical Journal [Brit. med. J.]* 2, 206–210, July 22, 1961. 21 refs.

Chlorthalidone, a sulphamyl benzophenone derivative and a new oral diuretic, was given at the Royal Victoria Infirmary, Newcastle upon Tyne, to 8 patients with fluid retention due to cardiac or hepatic failure and to 9 healthy controls. The action of the drug was very similar to that of chlorothiazide, but the diuretic effect. lasted much longer—18 hours in the controls and up to 72 hours in the patients. Excessive potassium loss, which also occurred, could be counteracted by potassium supplements or by the simultaneous administration of spironolactone. The only marked toxic effect was a rise in the blood urea level with large doses; this, however, fell after withdrawal of the drug. The authors recommend a dosage of 100 to 200 mg. once or twice a week for the treatment of oedema and 12.5 to 25 mg. every day as an adjuvant in the management of patients with hypertension. R. Schneider

38. Diuretics and the Eye

D. A. CAMPBELL. British Medical Journal [Brit: med. J.] 2, 467–474, Aug. 19, 1961. 14 figs., 29 refs.

Beginning with a study on migraine and diuretics, the author has interested herself for some years in the relationship of diuretics and intraocular pressure and the concurrent systemic biochemical changes. A close time relationship was found between the effect of carbonic anhydrase inhibitors on urinary excretion and the changes

in the intraocular pressure in glaucomatous patients. The period of hypotensive action coincided with the period of diuresis and of increased excretion of salts, particularly of sodium. In this paper from the Birmingham and Midland Eye Hospital the author summarizes her work, some of the results of which have been previously published.

She found that when acetazolamide is given in repeated daily doses its effect on the intraocular pressure steadily diminishes. This is associated with a decline in the excretion of bicarbonate, of sodium, and, to a less extent, of potassium. The loss of bicarbonate from the body is counterbalanced by the retention of chloride, and as a result a state of acidosis develops which may last as long as 48 hours and the eye becomes resistant. The addition of potassium bicarbonate in doses of 1 g. 3 times daily restores the efficacy of acetazolamide, which may then be used for years if kidney function is normal.

The systemic effects of chlorothiazide, aminometradine, urea, acetazolamide, and methazolamide were compared. Urea produced an increased urinary output and a corresponding fall in intraocular pressure; acetazolamide and methazolamide a moderate divresis and a sustained fall in intraocular pressure; aminometradine a moderate diuresis and no fall in intraocular pressure; and chlorothiazide a large diuresis and no effect on intraocular pressure. All the diuretics produced a fall in osmolarity of the blood, but the fall was significant only in the cases of acetazolamide and methazolamide. The diuretics acetazolamide, methazolamide, chlorothiazide, and urea caused a fall in the blood level of both sodium and bicarbonate, but the fall was again significant in the case of the carbonic anhydrase inhibitors, when it was compensated by a rise in the chloride level.

. It would appear that the glaucomatous subject retains sodium and exhibits a marked lability of the resting blood sodium level. It is possible that a reduction in the rate of sodium influx, which may in turn depend on the concentration of sodium in the plasma, will cause a fall in intraocular pressure in the glaucomatous eye, but will have no effect on the healthy eye. The changes in intraocular pressure are closely associated either with a disturbance in the acid-base balance of the blood, in which sodium plays a large part, or with alterations in blood osmolarity. To what extent these are interrelated is not yet known. There is evidence, however, that the ciliary body maintains an active transport of sodium, which must be of primary importance in determining the volume of intraocular fluid—that is, the intraocular pressure throughout the day. S.J.H. Miller

39. Clinical Experience with a New Sulphamyl Diuretic (G 33182: Chlorthalldone). (Klinische Erfahrungen mit einem neuen Sulfamyl-Diureticum (G 33182—Chlorthalldon))

W. SIMROCK. Chemotherapia [Chemotherapia (Basel)] 3, 1-24, 1961. • 4 figs., 30 refs.

The isoindolin derivative chlorthalidone ("hygroton") is a new, highly active, sulphamyl diuretic causing increased excretion of salt and water for up to 96 hours.

The effects of chlorthalidone correspond generally to those of chlorothiazide and its derivatives, particularly in regard to their anti-hypertensive properties. Changes in the serum electrolyte levels are similar in nature and frequency to those caused by chlorothiazide. The danger of hypokalaemia should in every case be avoided by giving potassium supplements by mouth. Azotaemia is not infrequent. Prolonged administration of large doses may cause side-effects. Although during a short course for the relief of oedema a strictly salt-free diet appears necessary, at least a little salt should be given in the diet during more prolonged treatment with chlorthalidone in order to prevent a high degree of salt depletion and its consequences.

Allergic or toxic side-effects have not yet been observed.

—[From the author's summary.]

40. Comparison of Hydroflumethiazide and Meralluride: New Method of Quantitative Assay of Directics in Bedfast Patients with Edema

H. GOLD, N. T. KWIT, C. R. MESSELOFF, M. L. KRAMER, A. J. GOLFINOS, D. MEHTA, W. ZAHM, and L. WARSHAW. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 239-242, July 29, 1961. 2 figs., 12 refs.

This paper reports the methods and results of a rapid quantitative comparison between the oral diuretic hydroflumethiazide and the mercurial diuretic meralluride sodium administered intramuscularly, the latter diuretic being used as the standard for comparison. The patient is kept at rest in bed, given a constant diet with salt intake restricted to approximately 2 g. daily, and digitalization carried out if there is congestive heart failure. The two diuretic agents (A and B) are given, in doses producing the maximum response, on 4 successive days, the order of administration being ABBA and BAAB. The measured response is the 24-hour weight loss, so that the sum: of the values for the test drug (T) on the 2 days is divided by the sum of the two values for the standard drug (S), yielding the ratio T:S, which represents the maximum diuretic potential of the test drug in terms of the standard. The average T:S ratio for a series of patients may then be examined by recourse to the appropriate statistical tests.

The 28 patients (18 male and 10 female ranging in age from 32 to 80 years) in the trial had oedema of between 7 and 68 lb. (3.18 to 30.8 kg.). In 12 cases the dose of hydroflumethiazide was 0.4 g. orally, but in the remaining 16 it was raised to 0.8 g.; meralluride was administered in intramuscular injections of 2 ml. Though there was a wide range of diagnoses, most of the patients had. congestive heart failure. The T:S ratio was 64.5% forhydroflumethiazide in doses of 0.4 g. and 68.7% for the higher dose. As there was no significant difference between the results of the two dosage levels, they were combined to give a ratio of 66.9%, the 5% confidence limits ranging from 53.1 to 80.7%. In 20 patients the organic mercurial was the more effective, in 4 hydroflumethiazide was more effective, and in 4 the two preparations showed no différence. In a previous report (Amer. J. med. Sci., 1960, 239, 665; Abstr. Wld Med., 1960, 28, 439) the authors showed that the T:S ratio obtained for chlorothiazide tested by the same method was 39.7%, with 5% confidence limits ranging from 26.3 to 53.1%. They therefore suggest that hydroflumethiazide is 1.5 to 2 times as effective as chlorothiazide for the clearing of oedema.

• R. H. Cawley

41. Placeho Responses in an Arthritis Trial R. A. H. Morison, A. Woodmansey, and A. J. Young.

Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 179-185, June, 1961. 2 figs., 15 refs.

A clinical trial of intra-articular injections of two steroid preparations in rheumatoid arthritis (Chandler et al., Lancet, 1958, 2, 661; Abstr. Wld Med., 1959, 25, 42), and in osteoarthritis (Wright et al., Ann. rheum. Dis. 1960, 19, 257) has already been recorded. The present paper reports the responses to the placebo injections which were used in the same trial.

Of the 49 patients with osteoarthritis or rheumatoid arthritis who were originally admitted, 39 (34 females, 5 males, age range 29 to 76 years) completed the 18month period of the trial. Each petient received 3 courses of injections, one course of each steroid and one of placebo, into the affected knee. Each course consisted of 4 injections with an interval of 2 weeks between injections; there was an interval of 2 months between courses. Walking time was eventually chosen as the most useful objective measurement; patients were tested fortnightly during the 2-month resting period following each completed injection course and the mean value was calculated as a percentage of the original walking time; decreases or increases of more than 10% were classified as improvement or deterioration. Patients were also asked to express their opinion regarding the value of the 3 courses on 2 occasions after completing them. Their claims were classified as unchanged, improved, and deteriorated. The two forms of hydrocortisone used, hydrocortisone acetate and hydrocortisone tertiary butyl acetate, did not differ significantly in their effect on the walking time, so for the purpose of the present study the mean of the two values recorded for both forms of steroid therapy was used for comparison with the values for placebo injections.

Of the 39 patients, 53% claimed to have improved with steroid therapy compared with 41% with the placebo; deterioration was reported by 10% and 8% respectively. With regard to walking time, 25% of patients improved with steroid therapy and 18% with the placebo; deterioration was recorded in 6% and 5% respectively. Thus both claims and findings indicated a slight superiority of steroids over placebo, but the differences are not statistically significant. The patients' claims showed a very constant pattern for each of the three courses; but the number of patients showing improved walking time after the first course greatly exceeded that after the second and third courses (19, 4, and 5 respectively). 'After completion of this trial all the patients were given a week's supply of dummy tablets and were asked to report the effects and to note undesirable effects. Ten claimed improvement, 12 claimed deterioration, and 16 indicated that they were unchanged; 16 reported side-effects. More favourable responses were recorded for injections

than for tablets (41% compared with 26%). All 16 patients who had had side-effects from the tablets had shown a placebo response of one or other kind, while none of the 11 patients who failed to respond in either trial reported side-effects. It was estimated that 29% of patients were non-responders to placebo, 37% occasional responders, and 33% regular responders. Preliminary reports of psychological investigations of placebo responders and non-responders are included.

R. H. Cawley

42. The Neuromuscular Blocking Properties of Certain Trophine Derivatives

J. P. PAYNE. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 278-284, June, 1961. 8 figs., 14 refs.

Competition block by tropine derivatives DF.596 and DF.648 has a similar mode of onset, duration of action and recovery period as suxamethonium, but these drugs are unlikely to be used clinically because of their tendency to alter the blood pressure, probably by ganglionic action.

Two observations were made which may be of experimental importance: (1) DF.596 produces a transient stimulating effect on the muscle twitch before the onset of neuromuscular block; (2) both drugs briefly enhance the action of decamethonium before antagonizing it, the effect becoming more marked with successive doses.—
[From the author's summary.]

43. A New View of Adrenergic Nerve Fibres, Explaining the Action of Reservine, Bretylium, and Guanethidine J. H. Burn. British Medical Journal [Brit. med. J.] 1, 1623-1627, June 10, 1961. 43 refs.

44. Mediated Acquisition of a Fear-motivated Response and Inhibitory Effects of Chlorpromazine. [In English]

W. M. DAVIS, J. CAPEHART, and W. L. LLEWELLIN. *Psychopharmacologia* [*Psychopharmacologia* (*Berlin*)] 2, 268-276, 1961. 15 refs.

The authors point out that while chlorpromazine is a valuable drug in the treatment of psychotic illnesses, it can also be useful in the less severe forms of psychiatric illness, and in this paper from the University of Oklahoma they describe animal experiments carried out on rats which may help in understanding the action of chlorpromazine in human patients suffering from neurosis. The experiments showed that the drug inhibits the acquisition and retention of responses motivated by conditioned fear. Wolpe and others have emphasized the place of such responses in the genesis of neurotic patterns of behaviour on man: On this theoretical basis the authors discuss the action of chlorpromazine in patients, with reference to the results of their own experimental work on animals, and suggest that in the treatment of the neuroses chlorpromazine is of value in "promoting the removal of unadaptive responses and the restoration of behavior appropriate to the circumstances", thus acting simultaneously to promote the B. M. Davies success of psychotherapy.

Chemotherapy

45. Pharmacology of Methicillin

P. ACRED, D. M. BROWN, D. H. TURNER, and D. WRIGHT. British Journal of Pharmacology and Chemotherapy [Brit. J. Pharmacol.] 17, 70-81, Aug., 1961. 4 figs., 9 refs.

The pharmacology of methicillin (6-(2:6-dimethoxybenzamido)-penicillanic acid) has been studied at the Beecham Research Laboratories, Betchworth, Surrey. Single intravenous doses of the antibiotic (2:5 g. per kg. body weight) in mice, single oral and subcutaneous doses (4 g. per kg.) in mice and rats, and repeated intramuscular doses in rats (0:5 g. per kg. daily for 12 weeks) and in dogs (0:25 g. per kg. twice daily for 4 weeks) produced no toxic effects. Intradermal injection of 0:1 ml. and 0:05 ml. of a 10% solution into rats and guinea-pigs respectively caused slight induration and erythema of the skin lasting 24 to 48 hours.

Oral doses of methicillin were shown to be poorly absorbed by rabbits and rats. After intramuscular injection the serum and tissue concentrations of methicillin in dogs and rabbits were similar to those found for benzylpenicillin. In the hen methicillin, like benzylpenicillin, is excreted through the kidneys by both renal tubular secretion and glomerular filtration. The concentration of methicillin in bile of both anaesthetized and conscious rats was higher than that found for benzylpenicillin, the ratio of bile concentration to blood concentration being 2.5 times that for the latter drug. About 75% of a dose of methicillin is excreted unchanged in the urine; the remainder is probably destroyed after passage through the bile into the intestine.

J. E. Page

46. Cyclophosphamide in Advanced Breast Cancer: a Clinical and Haematological Appraisal

B. A. STOLL and J. H. MATAR. British Medical Journal [Brit. med. J.] 2, 283-286, July 29, 1961. 6 figs., 9 refs.

In the development of cytotoxic agents for the treatment of cancer attempts have been made to widen the toxic: therapeutic ratio. Modifications of the basic compound, nitrogen mustard, have decreased the toxicity, and a new derivative, cyclophosphamide ("endoxan"), is claimed to have erythrocyte- and platelet-sparing properties.

Since November, 1959, 43 patients with advanced cancer have been treated with this drug at the Peter Mac-Callum Clinic, Melbourne, of whom 27 suffering from mammary carcinoma with measurable soft-tissue lesions, are considered in this paper. If there were no osseous or liver metastases a single massive intravenous dose was given at the rate of 45 to 50 mg. per kg. body weight; if such metastases were present, as they were in 9 cases, the dosage was reduced to 30 to 35 mg. per kg. If the patient was overweight relative to her height and build the lower limit of each dosage schedule was employed. When transient response occurred the treatment was repeated at two-thirds of the previous dosage after an

interval of 6 to 8 weeks, provided the patient's general condition was good. There were considerable toxic effects. Vomiting, which occurred in 21 of the 27 patients and was severe in 13, began between 6 and 10 hours after the injection and lasted for 4 to 6 hours. Dizziness was noted in 3 cases, sterile cystitis in one. and diarrhoea in one. The side-effect most troublesome to the patients was alopecia, which occurred in all cases, beginning in 3 to 4 weeks and resulting in 80% or more baldness in 10 cases, 25 to 75% in 8, and less than 20%. in 5 out of 23 cases followed up. The leucocyte count fell to below 1,000 per c.mm. in 11 out of 15 surviving patients; the fall occurred between the 7th and 13th days, but the count began to recover in a few days and was back to normal in 4 weeks. The platelet count remained unchanged in 13 cases, but showed a fall in 14 cases, in 8 of which it was slight, in 2 moderate, and ·in 4 marked.

Of 20 patients available for evaluation, objective tumour regression occurred in 7 and in a further 3 it was transient; the remaining 10 derived no benefit. In only one case could the response be described as excellent. In all cases control lasted for 2 months only. In half the cases a further short benefit was obtained when the treatment was repeated, but thereafter new metastases or recurrence of activity appeared. A comparison of the haematological effects in this series with those in another following treatment with thiotepa (triethylene thiophosphoramide) showed that cyclophosphamide had less damaging effects on haematopoietic tissues.

I. G. Williams

47. A Synthetic Amoebicide Capable of Replacing Emetine: 2-Dehydro-emetine. (Un amoebicide synthetique susceptible de remplacer l'émetine: la 2-déhydro-émétine)

F. BLANC, Y. NOSNY, M. ARMENGAUD, M. SANKALE, M. MARTIN, and G. CHARMOT. Presse médicale [Presse méd.] 69, 1548–1550, July 15 and July 22, 1961. 8 refs.

The authors report their experience with a recently synthesized form of emetine, 2-dehydroemetine, which is readily diffusible, rapidly eliminated, and has been shown to be less toxic and more effective than emetine both in animal experiments and in the treatment of patients with amoebiasis. The experiments showed that it is six times more active than emetine in infected rats and half as toxic as emetine in mice. Given in doses of 10 mg. per kg. body weight by intramuscular injection it has been found effective in the treatment of 134 cases of amoebiasis in Senegal, these including acute and chronic intestinal infections as well as primary and secondary hepatic infections. It does not produce mustee or tachycardia and the electrocardiogram remains unaltered.

If these findings are confirmed this new drug would appear to be safer and more effective than emetine.]

Clement C. Chesterman

Infectious Diseases

48. Paralytic Poliomyelitis in Massachusetts, 1959: a Study of the Disease in a Well Vaccinated Population S. Berkovich, J. E. Pickering, and S. Kibrick. New England Journal of Medicine [New Engl. J. Med.] 264, 1323-1329, June 29, 1961. 28 refs.

This paper from the Children's Hospital Medical Center and Harvard Medical School, Boston, and the Communicable Disease Center, Atlanta, Georgia, surveys further information regarding the efficacy of killed poliovirus vaccine provided by an outbreak of poliomyelitis (Type 3) in Massachusetts in 1959. On this occasion 62 (47%) out of 137 cases of paralytic poliomyelitis had been properly immunized (3 or more inoculations). Serologically a poor Type-1 and Type-3 antibody response was found both in patients (19) and in a selected laboratory staff group (21).

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Although both severity and mortality were considered to have been reduced as a result of immunization, the results were not satisfactory and the potency of the vaccine, especially with regard to its Type-3 content, was considered to be at fault. Mention is made of the lack of potency of Type 1 in earlier vaccines and a parallel is drawn here in the case of Type 3.

[This survey further emphasizes the care necessary in assessing immunization procedures and the importance of evaluating them rather than accepting their efficacy. Although the potency of present vaccines is not in the same doubt, future surveys will be necessary and the authors rightly re-emphasize that antibody levels are only an index of immunity and do not necessarily imply protection.]

Exercise 1.1.

**Exercise 2.1.*

**Exercise 3.1.*

**Exercise 3

 Vaccination against Poliomyelitis with Live Virus Vaccines.
 Changes in Sabin Type II Oral Vaccine Virus after Human Passage

D. S. DANE, G. W. A. DICK, M. BRIGGS, R. NELSON, J. McALISTER, J. H. CONNOLLY, M. HAIRE, F. McKEOWN, and C. M. B. FIELD. *British Medical Journal [Brit. med. J.]* 2, 259–265, July 29, 1961. 3 figs., 8 refs.

If and when the use of oral live poliovirus vaccines in poliomyelitis vaccination programmes is embarked upon on a large scale, many countries will wish to conduct field surveillance of the safety of the vaccine, as is at present being done in respect of the inactivated (Salk) poliovirus vaccine. The authors therefore report from the Queen's University of Belfast the results of a small trial with Sabin oral Type-2 attenuated poliovirus vaccine aimed at defining some of the more common changes that may occur in the virus after human passage.

The vaccine was first fed to 2 children, both of whom became infected, and then peak-titre faecal virus from one of them was given at various dilutions to 27 out of 33 children aged 5 to 17 months in a large ward of a children's home, the remaining 6 unvaccinated children serving as contacts. Of the vaccinated children, 4 showed evidence of a natural Type-1 infection, while a few had

some residual low-titre maternal antibodý. All the 9 children fed 1,000 TCD₅₀ became infected as a result of the feeding, but only 6 of those fed lower dosages did so. Subsequently 11 of the 12 children who did not excrete virus within the first few days and 5 of the 6 contacts became infected. No differences were observed between the average height or duration of virus excretion in the children infected by feeding and those infected by contact, and all developed neutralizing antibody to Type-2 poliovirus.

Peak-titre viruses representing the second, third, and possibly the fourth human passage were then tested for neurovirulence by intracerebral inoculation in rhesus monkeys. Whereas the original vaccine produced no paralysis and no histological lesions, the viruses which had undergone human passage produced limited paralysis in 6 and histological lesions in 16 of the 19 monkeys inoculated. The change to greater neurotropism appeared to be progressive up to 5 weeks, but virus recovered after 15 weeks' multiplication in the intestinal tract showed no higher neurotropism. Comparison of the t (temperature) marker character, that is, the increased ability of a strain to multiply at 40° C. believed to be associated with increased neurotropism, was found to be of limited value in differentiating the humanpassaged viruses from virulent poliovirus. Tests for the d marker, that is, the ability of certain virus strains to form plaques in the presence of a low bicarbonate concentration in the overlay medium, showed that some of the human-passaged viruses were $d\pm$, whereas the original virus was d-. None of the viruses tested could be distinguished from each other antigenically.

It is concluded that there appeared to be no differences between the infectivity of the virus after the first human passage and that of the original vaccine virus, while community surveillance, which formed part of the trial, indicated that no case of paralytic poliomyelitis due to Type-2 poliovirus occurred in Northern Ireland in the year following the trial.

A. Ackroyd

 Vaccination against Pollomyelitis with Live Virus Vaccines.
 Effect of Previous Salk Vaccination on Virus Excretion

G. W. A. DICK, D. S. DANE, J. McALISTER, M. BRIGGS, R. NELSON, and C. M. B. FIELD. *British Medical Journal [Brit. med. J.]* 2, 266–269, July 29, 1961. 5 figs., 13 refs.

The authors report from the Queen's University of Belfast the results of an investigation into the problem of whether the large-scale use of formalin-inactivated poliomyelitis vaccine can affect the circulation of polioviruses in a community.

In the first trial 16 young non-immune children were given 2 doses of Salk vaccine one month apart, and then 2 weeks later they and 16 control children were fed 10^{5.6} TCD₅₀ of live Sabin Type-2 attenuated poliovirus

vaccine. No differences in the geometric mean titre of faecal virus excreted by the two groups of children were , part the children were less than 8 years old. The virus observed. In the second trial 2 or 3 doses of a more potent Salk vaccine were given to 10 young children and then 2 weeks later they and 9 paired control children were fed 106 TCD50 of Sabin Type-1 virus. Some of the children had previously been shown to have antibody to Type-2 virus. Virus was excreted in the faeces in smaller amounts and for a shorter duration by the Salk-vaccinated group, while virus was not excreted in the throat at all by any of the children with Type-1 antibody following Salk vaccination. The authors point out that this finding conflicts with the hypothesis that a purely local immunity is the only mechanism producing intestinal resistance. A. Ackroyd

51. Vaccination against Poliomyelitis with Live Virus Vaccines. 8. Changes in Sabin Type I Oral Vaccine Virus after Multiplication in the Intestinal Tract

D. S. DANE, G. W. A. DICK, M. BRIGGS, R. NELSON, J. McAlister, J. H. Connolly, F. McKeown, and C. M. B. FIELD. British Medical Journal [Brit. med. J.] 2, 269-271, July 29, 1961. 1 fig., 3 refs.

Faecal and, in 4 cases, throat viruses isolated from 8 out of 11 children 1 to 5 weeks after being fed 106 TCD₅₀ of Sabin Type-1 attenuated poliovirus and from 3 of their contacts were tested for neurovirulence in monkeys by intracerebral inoculation and for any changes in the t and d marker characters [see Abstract 49].

In contrast to the original vaccine virus, the humanpassaged strains produced paralysis in 7 and histological lesions in 16 of the 20 monkeys inoculated, but neither the paralyses nor the lesions were as severe as is usually the case when virulent strains are tested in this manner. None of the 44 strains isolated after varying periods of growth up to 5 weeks in the human intestinal tract were t+, and only 3 strains were $t\pm$, but when the test was performed at 39° C. 7 of the 19 strains tested were t+. There was a tendency for viruses to have greater ability to multiply at 39° C. the longer they had multiplied in the intestinal tract. Some change in the d marker character of the human-passage strains was also observed.

While no case of paralytic poliomyelitis due to Type-1 poliovirus has occurred in Northern Ireland since the Type-1 vaccine virus was fed, there have been 5 such cases due to Type-3 virus which was imported from a town in England where some months earlier all three types of attenuated poliovirus vaccines had been fed to a small number of children. Cases of acute poliomyelitis due to Type-3 virus had occurred elsewhere in England earlier in the year. A. Ackroyd

52. Measles Vaccine

S. KARELITZ, F. DESPOSITO, S. GITTELSON, H. GOLDMAN, A. Ross, F. S. MARKHAM, J. M. RUEGSEGGER, and H. R. Cox. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 537-541, Aug. 26, 1961. 10 refs.

At Long Island Jewish Hospital, New York, clinical and serological observations were made on 103 children who were given subcutaneous injections of the Edmonston strain of attenuated measles virus. For the mosthad been propagated in tissue cultures of chick embryo and passaged in primary human amnion and kidney cells. Three preparations of the virus were employed, each child receiving 1 ml. of reconstituted vaccine.

Transitory pain at the site of injection was recorded in 10 cases, but generalized toxic or allergic reactions were not observed. Febrile episodes occurred in 40 cases, with temperatures ranging from 100.2° to 104° F. (37.9° to 40° C.) for an average period of 3 days. In 10 children the degree of fever was as severe as that of the naturally acquired disease. Within 7 to 12 days of vaccination a sparse macular rash appeared in 20 of 72 children who were serologically negative for measles virus antibodies; in 10 cases its distribution was limited to the face and neck. The rash remained in evidence for an average period of 2.2 days, but was never as vivid as the rash of naturally acquired measles. Lesions resembling Koplik's spots were seen in 7 children. The clinical response also included coryza, cough, conjunctivitis, and pharyngitis; 3 children suffered from mild attacks of otitis media and there were 2 cases of bronchitis. Encephalitic signs were never encountered.

Serological tests revealed that in a group of 86 children who had been non-immune, vaccination had led to a degree of immunization comparable to that produced by an attack of ordinary measles. No secondary cases of measles were observed in the parents or in susceptible siblings in contact with the children. A. Garland

53. 'Living Attenuated Measles-virus Vaccine in Early Infancy: Studies of the Role of Passive Antibody in Immunization

C. M. REILLY, J. STOKES JR., E. B. BUYNAK, H. GOLDNER, and M. R. HILLEMAN. New England Journal of Medicine [New Engl. J. Med.] 265, 165-169, July 27, 1961. 7 refs.

The aims of this study from the University of Pennsylvania School of Medicine, the Children's Hospital of Philadelphia, and the Merck Institute for Therapeutic Research, West Point, Pennsylvania, were to determine whether: (a) there was any induced immunity in infants inoculated with Enders's living attenuated measles virus vaccine who initially possessed measurable maternal antibodies; (b) whether older infants with mild infection who were initially devoid of antibody but who had responded serologically to vaccination were immune to reinfection with an attenuated measles virus vaccine of higher titre; (c) whether higher-titre vaccine could infect young infants with a low titre of maternal antibodies; and (d) whether human γ globulin given immediately after the live vaccine would reduce the severity of the vaccine-induced disease while still permitting an immune response. . . .

Nine infants vaccinated in a study 7 to 9 months previously were revaccinated with high-titre measles virus vaccine. Four who had been initially seronegative and had responded to vaccination still had antibodies at the time of the second dose and did not become infected. The remaining 5 had been seropositive initially and had failed to respond to the first vaccination; all were

successfully vaccinated on the second occasion. Four of these were given a modifying dose of γ globulin and developed no clinical symptoms or signs; the other infant had a mild clinical reaction.

Of 14 infants who were given primary vaccination with the high-titre vaccine, 9 were susceptible (that is, they had no maternal antibody). Six of these were given y globulin, 2 of whom developed no clinical illness, while 4 showed a mild clinical reaction on the 5th to 8th day after vaccination; the remaining 3 developed postvaccination reactions. All these 9 developed a typical response of neutralizing and complement-fixing antibodies, whereas the 5 who had maternal antibodies showed neither serological nor clinical response. Thus in the presence of maternal antibodies there was no clinical or serological response to live measles virus vaccine, irrespective of the potency of the vaccine used. while y globulin was shown to be capable of reducing the clinical reaction to vaccination without influencing antibody response.

[These results correspond with those of other, similar studies (see McCrumb et al., Amer. J. Dis. Child., 1961, 101, 708; Abstr. Wld Med., 1961, 30, 363).]

Kurt Schwarz

54. Action of Steroid Therapy in Jaundice R. WILLIAMS and B. H. BILLING. Lancet [Lancet] 2, 392-396, Aug. 19, 1961. 3 figs., 21 refs.

The effect of steroid therapy on bilirubin metabolism was studied in infective hepatitis and other forms of jaundice. In hepatitis responding to prednisolone, two distinct phases were noted: a rapid drop in serum-bilirubin in the first 24 to 48 hours, followed by a very much slower fall. In contrast, in patients recovering without steroid treatment there was a single rate of clearance. In obstructive jaundice the fall in serum-bilirubin level was less marked, and when treatment was discontinued the value promptly returned to the initial level.

The response in obstructive jaundice and the initial fall in infective hepatitis could not be accounted for by increased biliary excretion, changes in renal clearance of bile-pigments, or decrease in the rate of red-cell breakdown. It was concluded that steroid therapy must cause or enhance the excretion of bilirubin via an additional metabolic pathway:—[Authors' summary.]

55. The Treatment of Acute Hepatitis with Vitamin B_{12} . (Die Behandlung der akuten Hepatitis mit Vitamin B_{12})

L. KELEMEN, C. HADNAGY, D. SZILÁGYI, and A. PALENC-SÁR. Internationale Zeitschrift für Vitaminforschung [Int. Z. Vitaminforsch.] 31, 307–316, 1961. Bibliography.

The authors describe the results of treatment of 379 patients with acute viral hepatitis at the University Clinic for Infectious Diseases, Marosvasarhely, Rumania. Of these patients, 140 were given 2,000 μ g. of vitamin B_{12} (cyanocobalamin) weekly [daily dose unstated], another 49 received a total of 1,000 μ g. weekly, while the remaining 190 were given no vitamin B_{12} and served as a control group. There was otherwise no difference in the dietetic and other medical management of the three groups of

patients, who were all moderately ill [criteria unstated]; severely ill patients were given blood plasma, cortisone, and ACTH and were not included in the trial. The results of treatment were assessed by the decrease in the degree of jaundice, bilirubinuria, urobilinogenuria, and the duration of the illness.

In the control group subjective symptoms ceased after 12.6 days compared with 11.1 days for those given the smaller dose and 9.8 days for those given the large dose of the vitamin. The times for disappearance of the jaundice in the three groups were 14.5, 12.1, and 9.9 days respectively, while bilirubin disappeared from the urine after 14.5, 10.9, and 8 days respectively. The total duration of illness showed a similar sequence, the periods for the three groups being 24, 19, and 10 days respectively.

The authors conclude [obviously enough] that on the above criteria the patients given vitamin B_{12} recovered more rapidly than the controls and that the most effective dose was one of 2,000 μ g. per week. There was, however, no difference in the rate of diminution in the size of the liver and spleen as between the controls and the vitamin-treated cases. The paper concludes with a review of the mechanism of action of vitamin B_{12} , in spite of which, however, this still remains unknown.

I. M. Librach

56. The Actiology of Pneumonia in Children with Pertussis. (К вопросу этиологии пневмонии у-детей больных коклюшем)

E. S. KUNCMAN, V. D. LJUBIMOVA, and N. D. GUSAROVA. Bonpocu Oxpahu Mamepuhcmaa u Hemcmaa [Vop. Ohrany Materin. Dets.] 6, 38-43, July, 1961. 1 ref.

The authors have compared the bacteriological findings in 100 children with pertussis complicated by pneumonia with those in 20 similar patients without this complication. Of these, 88 were admitted with a diagnosis of pneumonia (16 of them with a recurrence) and in the other 12 it was found to be present on admission.

Streptococcus viridans was isolated in 99 of the pneumonia cases and in 17 of the controls, being recovered on several occasions in both groups during the period in hospital. Pfeiffer's bacillus (Haemophilus Influenzae) was found in 70 of the pneumonia cases and in 12 of the controls. The organisms which were more frequent in the children with pneumonia than in those without were staphylococci, pneumococci, and yeast-like organisms. It is suggested that the prevalence of the last-named was probably due to the use of antibiotics in the patients with pneumonia; in no case were they the dominant microflora. In 41 cases the predominant organisms were pathogenic staphylococci and in 10 pneumococci; in only 4 children with primary pneumonia was Pfeiffer's bacillus the dominant organism. Strept. viridans was the . dominant organism in 22 of the pneumonia cases and in 8 of the controls, the evidence seeming to suggest that it is not the pathogenic organism, but is a normal inhabitant of the respiratory tract. The main pathogenic organisms seem to be pathogenic staphylococci and pneumococci. In recurrences of pneumonia they were the only predominant pathogens.

L. Firman-Edwards

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Tuberculosis

57. An Outbreak of Primary Tuberculosis in School Children. Clinical Aspects

S. C. F. MAHADY. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 348-358, Sept., 1961. 2 figs., 7 refs.

When active pulmonary tuberculosis was diagnosed in the driver of a school bus in Utica, New York, intradermal tuberculin tests, chest radiography, and gastric lavage were carried out on the pupils of the school concerned. All non-reactors to the tuberculin test were re-examined after an interval of 3 months. Positive tuberculin reactions were obtained in 85 (32%) of 266 students who had travelled in the bus (exposed group) and in 60 (1.8%) of 3,401 other pupils of the school (non-exposed group). Radiological examination showed that 52 out of the 85 children in the exposed group had active primary tuberculosis and 6 had healed primary lesions, whereas 4 out of the 60 children in the nonexposed group, had active tuberculosis and 24 had evidence of a healed primary complex. Drug therapy, which was recommended for 69 of the 85 reactors in the exposed group, was given to 65 as follows: isoniazid to 39, isoniazid and PAS to 13, and isoniazid, PAS, and streptomycin to 13. Only 5 of the non-exposed group received drugs-isoniazid to 4, and isoniazid, PAS, and streptomycin to one. Treatment was continued for at least 12 months, in some patients for 2 years. The response to treatment was satisfactory except in a few patients who did not complete the course or who were sensitive to the drugs. There was almost complete clearing of the lesions radiologically after 18 months.

R. M. Todd

58. Tuberculin Testing of School Children W. N. B. WATSON and J. WILLISON. Medical Officer [Med. Offr] 106, 83-87, Aug. 4, 1961. 10 refs.

Since 1954 children under the age of 14 attending schools in Edinburgh have been tuberculin-tested whenever infectious tuberculosis was notified in a school-child or adult school worker. Between 1954 and 1960 2,263 children were tested as the result of 37 infectious cases having been reported. In 36 of these no dissemination of infection was found, but in the remaining case, in a girl aged 13 at a small independent school, 11 (61%) of her 18 classmates were shown to be tuberculin-positive and 4 had active tuberculosis.

Since 1957 some 2,600 children aged 5 years have been given routine tuberculin tests; of these, 32 gave a positive tuberculin reaction and one of them had manifest tuberculosis. In 1958 the scheme was extended to cover all age groups in primary schools and about 4,000 children (aged 5 to 12 years) were tested. Among these, 3 active cases of tuberculosis were discovered, but none were found among the 454 home contacts who agreed to undergo x-ray examination. In 1959 2,231 children were re-

tested after an interval of one year, when it was found that 4 had converted but none had active disease. Since B.C.G. vaccination of children in their 14th year was instituted 0.3 per 1,000 vaccinated children have developed tuberculosis as compared with 8.4 per 1,000 children with naturally acquired tuberculin sensitivity.

T. M. Pollock

59. Heocecal Tuberculosis with Particular Reference to Isolation of Mycobacterium tuberculosis. With a Note on Its Relation to Regional Heltis (Crohm's Disease)
K. L. Wig, N. L. Chitkara, S. P. Gupta, K. Kishore, and R. L. Manchanda. American Review of Respiratory Diseases [Amer. rev. resp. Dis.] 84, 169-178, Aug., 1961. 6 figs., 12 refs.

This paper from the Medical College, Amritsar, India, reports a study of 67 patients with intestinal tuberculosis seen between 1953 and 1957. There were 50 females and 17 males whose ages ranged from 13 to 50 years, though most (54) were aged 15 to 34 years. Symptoms had been present for 12 days to 20 years and the usual complaint was of dull abdominal pain with short attacks of meteorism. In 49 cases a palpable mass was present in the right iliac fossa, in 7 mesenteric lymph nodes were felt, intestinal obstruction was observed in 12, ascites was found in 4, and enlarged extra-abdominal lymph nodes discovered in 13. All patients were Mantouxpositive, the erythrocyte sedimentation rafe was raised in 48, active pulmonary tuberculosis was present in 4, inactive pulmonary tuberculosis in 14, pleural thickening in 2, and enlarged mediastinal lymph nodes in 10. In only one case were tubercle bacilli grown from the sputum, and this was after gastric lavage. Barium radiological studies of the bowel were performed on 60 patients. A persistent filling defect in the region of the caecum, sometimes extending to the terminal ileum or ascending colon, was seen in 42 patients, while 12 patients showed the signs of small-intestinal obstruction.

A laparotomy was performed in 56 cases with the following findings: thickening of the caecum and adjoining portion of the ascending colon and terminal ileum in 23; thickened caecum alone in 6; small-bowel strictures with ileocaecal involvement in 11; small-bowel strictures without ileocaecal involvement in 13; and enlarged mesenteric lymph nodes alone in 3. A short-circuit operation was carried out on 47 patients, but was impracticable in 6 cases. A hemicolectomy was performed later, after chemotherapy, in 16 cases.

Of 55 specimens of mesenteric lymph nodes examined histologically, 38 were tuberculous, while all of 10 specimens of extra-abdominal lymph nodes were tuberculous. The intestines were examined in 36 cases; all showed thickening of the wall in the diseased areas with infiltration with round and plasma cells; in 2 there was cosinophilic infiltration and in 4 follicles with epithelioid and giant cells. Tubercle bacilli, all human type, were grown

from the mesenteric lymph nodes in 4 cases, from the intestinal wall in 6, from the axillary lymph nodes in 4, from ascitic fluid in one, and from menstrual blood in one. The 49 patients with ileocaecal tuberculosis were of special interest in that 31 showed a tuberculous histology, but tubercle bacilli were grown in only 15 cases, the culture being negative in 16. In 5 cases the histology was not specifically tuberculous, but tubercle bacilli were isolated on culture, and in the remaining 13 there was neither a definitely tuberculous histology nor a positive culture.

The authors remark that the 5 patients with a positive culture but negative histology are of great interest since they show that tuberculosis of the caecum does not always cause caseation necrosis and in the absence of a positive culture a diagnosis of Crohn's disease could have been made. The same is true of the 13 patients in whom neither the histology nor the culture were positive because the clinical picture, macroscopic findings, and course were similar to those observed in the confirmed cases. They conclude that hyperplastic ileocaecal tuberculosis is less uncommon (at least in India) than is usually believed and that it probably accounts for "a fairly large number" of cases of Crohn's disease.

Arthur Willcox-

RESPIRATORY TUBERCULOSIS

60. The Level of Residual Free Isoniazid in the Serum and the Therapeutic Results in 104 Previously Untreated Cases of Pulmonary Tubérculosis. (Taux d'I.N.H. libre résiduel et résultats thérapeutiques chez 104 tuberculeux pulmonaires "neufs")

E. Bernard, L. Israël, D. Pariente, and J. Sausy. Revue de tuberculose et de pneumologie [Rev. Tuberc. (Paris)] 25, 319–338, April [received Aug.], 1961. 3 figs., 23 refs.

In this study undertaken to confirm the value of high doses of isoniazid (15 mg. per kg. body weight) the authors have compared the clinical results with the level of residual free isoniazid in the serum of 104 patients with pulmonary tuberculosis, not previously treated, who were given daily 15 mg. of isoniazid per kg. body weight, 15 g. of PAS intravenously, and 1 g. of streptomycin intramuscularly. By means of a vertical tube diffusion method the level of active isoniazid in the serum was determined 5 hours after a dose of 4 mg. of isoniazid per kg. On this test the patients were divided according to the serum level of isoniazid into three groups: (1) rapid inactivators (serum level 0 to 0.5 μ g. per ml.); (2) moderately rapid inactivators (serum level 0:5 to 2 μ g. per ml.); and (3) slow inactivators (serum level over $2 \mu g$. per ml.). The distribution in these three groups was 29.8, 34.7, and 35.5% of the patients respectively.

At the end of 3 months of the treatment regimen described above there was radiological clearing in 54.8% of the cases in Group 1, 75% in Group 2, and 83.7% in Group 3. At 2 months the sputum had become negative in 48, 65, and 70% in the three groups respectively, but at 3 months these differences had disappeared. Only 3 patients showed toxic symptoms affecting the central nervous system and all 3 had a previous history of

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psychological disturbances. The authors conclude that the risk of neurotoxic accidents depends more on the individual patient's previous psychiatric history than on the dose of isoniazid employed.

G. M. Little

61. An Investigation of the Value of Ethionamide with Pyrazinamide or Cycloserine in the Treatment of Chronic Pulmonary Tuberculosis

A REPORT FROM THE RESEARCH COMMITTEE OF THE BRITISH TUBERCULOSIS ASSOCIATION. Tubercle [Tubercle (Lond.)] 42, 269–286, Sept., 1961. 1 fig., 19 refs.

Patients admitted to this trial of ethionamide with pyrazinamide or cycloserine in the treatment of chronic pulmonary tuberculosis were drawn from 13 hospitals and were selected because either sputum cultures grew tubercle bacilli resistant to streptomycin, PAS, and isoniazid or the patients were thought to be resistant since they had failed to respond to these drugs. In all the patients sputum was positive on smear on two consecutive occasions within a fortnight before the start of treatment, and at least one lung cavity was present at the beginning or was known to have existed shortly before. Treatment regimens were not allocated at random because of the objection of some doctors to the use of pyrazinamide; doctors were therefore at liberty to choose combinations of either ethionamide and pyrazinamide or ethionamide and cycloserine. Chemotherapy was given for 6 months in the first place, but could be extended to 12 months or more. There were two treatment groups: (1) the EZ group who received ethionamide in a dosage of 0.5 g. daily by mouth (in entericcoated tablets) plus pyrazinamide in a dosage of 2 g. daily for patients weighing less than 50 kg., 2.5 g. daily for those weighing 50 to 63 kg., or 3 g. daily for those weighing over 63 kg.; (2) the EC group, who received ethionamide (as in the EZ group) and cycloserine in a dosage of 0.5 g. daily for patients under 50 kg. weight, 0.75 g. daily for those 50 to 69 kg., and 1 g. daily for those weighing over 69 kg.

Before treatment began two specimens of sputum from each patient were examined and tested for sensitivity, a chest radiograph was obtained, the urine was examined for protein, urobilinogen, and bile, and the common liver function tests were carried out. During treatment (at least 3 months of which, if possible 6 months, was given in hospital) these investigations were repeated an regular intervals. All observations were recorded monthly and sent to the coordinating centre for study and collation.

Sputum was examined by smear and culture and a negative result was defined as "3 or more consecutive weekly negative results or 2 negative results if only 2 specimens were available in any one month, or a single negative result in 2 consecutive months where only one monthly sputum was available". Sensitivity tests for ethionamide and cycloserine were carried out on You-mans's medium and cultures were regarded as having reduced sensitivity if they showed greater resistance ratios than 99% of a series of pre-treatment cultures.

After the exclusion of 12 patients for various reasons a total of 62 remained in the trial—36 in the EZ group

and 26 in the EC group. Of the 36 patients in the EZ group, 27 completed 3 months' treatment in hospital and 18 completed 4 months; at the end of 5 months 11 remained in hospital and at the end of 6 months 8 remained. In the EC group 21 patients completed 3 months in hospital, and at the end of the fourth, fifth, and sixth months respectively only 17, 14, and 11 patients remained. At the end of 3 months' treatment 14 of the 27 patients in the EZ group who were still receiving the drugs had negative sputum on smear and culture; in the EC group 13 of the 21 patients had negative smears and 16 had negative cultures. Of 16 patients in the EZ group and 20 in the EC group still under treatment, 9 and 14 respectively had negative cultures; after 9 months' treatment the corresponding figures were 8 out of 10 in the EZ group and 8 out of 12 in the EC group. All 7 patients in the EZ group and 7 of the 11 in the EC group who completed twelve months' treatment were sputum-negative.

Evidence was obtained of reduced sensitivity to ethionamide before the start of treatment in 5 of the 48 strains tested (3 in the EZ group and 2 in the EC group), to pyrazinamide in 2 of the 26 strains tested, and to cycloserine in one of the 20 cultures tested. In the EZ group all patients showing apparent resistance before treatment remained sputum-positive, and resistance to the second drug developed by the third to fifth months of therapy. In the EC group all 3 patients in whom reduced sensitivity was observed before treatment began became sputumnegative after 2 months' treatment and remained so thereafter. Resistance to ethionamide and pyrazinamide developed most commonly with less than 3 months' treatment, but ethionamide resistance was seldom observed before 6 months when this drug was given with cycloserine. Resistance to cycloserine occasionally developed after 9 months' treatment.

It was not possible to determine whether any acute hypersensitivity reactions to the drugs occurred and no hypersensitivity to pyrazinamide or cycloserine was recorded. In the EZ group 9 patients showed liver damage as assessed by the results of liver function tests and in 2 of these clinical jaundice developed. There was some evidence in 4 patients of apparent failure of absorption of ethionamide in enteric-coated tablets.

It is concluded that neither combination of these drugs in the dosages given in the trial is completely effective in advanced pulmonary tuberculosis, but the demonstration that just over half the patients who continued treatment had negative cultures at 6 months encourages further investigation.

W. Raymond Parkes

62. Absorption and Tolerance of Large Single Doses of Kabipastin, a para-Aminosalicylic Acid Ion Exchange Resin Combination. [In English]

O. Selroos. Acta tuberculosea Scandinavica [Acta. tuberc. scand.] 40, 222-236, 1961. 5 figs., 13 refs.

In view of the gastric intolerance long observed with the taking of PAS preparations the author tried "kabipastin", which is a p-aminosalicylic acid ion exchange resin compound, in the treatment of tuberculosis at Mjölbollstad Sanatorium, Finland. In single doses of

24 g. this drug gave results comparable with those obtained with the usual PAS compounds. The drug was well tolerated within this range of dosage. The author considers that kabipastin may well have a place in the treatment of tuberculosis in cases where the usual PAS compounds give rise to abdominal discomfort.

Paul B. Woolley

63. Ambulatory Treatment of Tuberculosis. Results in 105 Tuberculous Patients Treated with Chemotherapy and Active Physical Rehabilitation

J. A. WIER, J. M. SCHLESS, L. E. O'CONNOR, and O. L. WEISER. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 17-22, July, 1961. 5 refs.

A therapeutic trial of exercise rather than rest as suitable treatment for pulmonary tuberculosis is reported from Fitzsimons General Hospital, Denver, Colorado. A series of 105 patients, 65 of whom had moderately or far advanced disease and 46 demonstrable cavitation, were treated with isoniazid and PAS, together with streptomycin in a limited number of cases. At the same time they took part in active callisthenics such as are given to regular troops during their basic training period.

Cavity closure was achieved in 20 cases with drugs alone. Considerable radiological improvement occurred and all patients were sputum-negative before their discharge from hospital, though 29 required additional surgical treatment to achieve sputum conversion. There has so far been no lengthy follow-up of these cases.

J. Robertson Sinton

64. Management of Pulmonary Tuberculosis during Pregnancy

R. B. PRIDIE and P. STRADLING. British Medical Journal [Brit. med. J.] 2, 78-79, July 8, 1961. 17 refs.

In an effort to reach some logical conclusions on the management of tuberculous patients during pregnancy, about which there is still a considerable divergence of opinion, a retrospective study of 103 pregnancies in 73 women with pulmonary tuberculosis active within the previous 5 years was undertaken at the Hammersmith Chest Clinic, Postgraduate Medical School of London. Of 46 women who had originally received chemotherapy for the treatment of the tuberculosis, 3 (7%) broke down during pregnancy, whereas of 57 women who had not received previous chemotherapy, 17 (30%) did so. Again, none of the 28 patients receiving chemotherapy during pregnancy broke down, compared with 20 (27%) of the 75 who received no chemotherapy during this time. There was no difference in the relapse rate between those who rested in bed for at least one month before delivery. and those who did not, but the number resting (14) was too small to allow of any definite conclusions on this point.

The authors conclude that the pregnant woman with pulmonary tuberculosis showing any signs of recent activity can undertake pregnancy and labour safely provided that she receives adequate chemotherapy, that rest in bed is not necessary, and further that non-infectious patients can safely breast-feed their infants.

G. M. Little

Venereal Diseases

65. The Immunity of the Central Nervous System in Endemic Syphilis. (Die Immunität des Zentralnervensystems bei endemischer Syphilis)

A. LUGER and E. E. SCHMID. Dermatologische Wochenschrift [Derm. Wschr.] 143, 617-637, June 17, 1961. 1 fig., bibliography.

The relevant literature is reviewed and the authors report their own experience in a series of 137 patients with endemic syphilis in Syria. No clinical evidence of neurosyphilis was found and the cerebrospinal fluid (C.S.F.) was normal in all patients except one in whom a weakly positive V.D.R.L. reaction was thought to be due to passive transfer of reagin from the blood to the C.S.F. The mechanism of the apparent immunity of the central nervous system in endemic syphilis is not known, but it is suggested that it may be due to the repeated superinfections known to occur in populations living in hyperendemic areas. It is also pointed out that cutaneous relapses are not seen in the course of endemic syphilis in contrast to venereal syphilis and that this difference indicates a different level of immunity in the two forms of syphilis. G. W. Csonka

66. Further Investigation into the Origin of Toxic Reacting Sera in the Treponental Immobilization (Nelson) Test. The Effect of Bacteria on Treponenta pallidum. (Weitere Untersuchungen liber die Ursache der toxisch reagierenden Seren im TPI-Test (Nelsontest). Die Wirkung von Bakterien auf das Treponema pallidum) B. ETTIG. Dermatologische Wochenschrift [Derm. Wschr.] 143, 673-676, July 1, 1961. 4 refs.

In a previous investigation carried out at the University Skin Clinic, Jena (Rietschel and Ettig, Derm. Wschr., 1961, 143, 241; Abstr. Wld Med., 1961, 30, 104) it was found that certain vulcanization accelerators used in the manufacture of rubber stoppers had a toxic effect sera used in the treponemal immobilization (T.P.I.) if Nelson. However, even after the substitution of for rubber it was noted that certain sera soon betoxic and it was decided to investigate the possithat this was due to bacterial contamination. preliminary studies it was found that certain bac-

when added to serum had a detrimental effect on test, whereas others had no such effect. In a sysatic survey 7 common bacterial species and 7 species ich were isolated from contaminated sera were added T.P.I.-negative serum. It was found that even small additions of Staphylococcus aureus or Proteus vulgaris resulted in 100% non-specific immobilization. On the other hand Bacillus mesentericus, Pseudomonas pyocyanea, and some of the unidentified contaminants had little effect on the T.P.I. test result. The addition of streptomycin to the serum in a concentration of 5 mg. per 0.5 ml. controlled contamination without adversely influencing the T.P.I. test and this practice has now been adopted as a routine measure. G. W. Csonka

67. General Paralysis of the Insane Today. (Die Progressive Paralyse heute)
N. VURDELJA, S. VUCKOVIĆ, and B. KAPAMADZIJA. Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.] 202, 177-182, 1961. 5 refs.

During the past 10 years 196 patients with general paralysis of the insane were admitted to the Neuropsychiatric Branch of the Novi Sad District Hospital, Jugoslavia. These patients constituted 5.4% of all first admissions during this period, indicating that in Jugoslavia general paralysis is less of a rarity than it has become in other countries. The illness was of gradual onset in 132 cases and of sudden onset in 64. The predominant symptoms at the time of admission were those of simple dementia in 89 cases, confusion in 34, euphoric dementia in 21, depressive state in 20, expansive syndrome in 15, paranoid state in 6, and various other conditions in 19. The authors point out that the clinical picture appears to have changed in that the classic syndrome of delusions of grandeur has become considerably less frequent than in the past, the expectation of life has markedly increased, and the severe dementias are much rarer. They believe that these changes are due to the influence of the changed socio-economic milieu on the form of the disease and to the occurrence of a higher proportion of cases of cerebral syphilis with a predominantly meningovascular as opposed to a predominantly parenchymatous reaction. J. Hoenig

68. Treatment of Acute Gonorrhea in Males with Synnematin B

B. Schwimmer, N. D. Henderson, and B. J. Olson. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] 76, 630–632, July, 1961. 6 refs.

Synnematin B, an antibiotic produced by the mould Cephalosporium salmosynnematum, Strain 3590 A, and known to be somewhat related to penicillin, is treponemicidal and markedly lethal to Nelsseriae. It is not, however, readily available. The authors of this paper from the Detroit and Michigan Departments of Health describe a trial of synnematin B on 132 males with proved (smear and culture) acute gonorrhoea. All the patients were given one intramuscular injection of 300,000 units of synnematin B. There were frequent complaints of local pain but no allergic reactions. Within 30 days 17 (13%) of the patients again had positive smears and cultures, but according to the criteria adopted only 5 (4%) were considered treatment failures, the others being considered to have a reinfection.

The results are compared with those in a random series of 100 similar patients treated with 1,200,000 units of penicillin. In this group 8 patients had a recurrence within 30 days, but only one was considered a treatment failure. The authors state that synnematin B appears to have great promise in the treatment of acute gonorrhoea.

Leslie Watt

Tropical Medicine

69. A Study of Vadrine, Alone and Combined with Sulphetrone

R. Brechet and R. G. Cochrane. Leprosy Review [Leprosy Rev.] 32, 180-187, July, 1961. 1 fig., 1 ref.

During the period 1955-60 "vadrine" (2-pyridyl-(4)-1:3:4-oxydiazalone-(5)p-aminosalicylate) was used in Angola to treat 40 patients with leprosy for 18 to 50 months and in this paper a report is presented on the 20 lepromatous cases in the series. The average dose was 30 mg. per kg. body weight daily. Lepromatous reactions occurred in 6 patients and mild reactions in another 6, while mild anaemia appeared in 8, severe anaemia in one, and nephritis in one. A sensation of burning in the legs and feet occurred in 8 patients during the 2nd and 3rd years. The clinical response was good in most cases and bacilli showed changes in form and became beaded. Histological improvement was also noted after the first year. During the second year improvement was less spectacular, but progress continued slowly. At the end of the second year the results were classified as "excellent" in 3 patients, "good" in 4, "satisfactory" in 7, "stationary" in 5, and "bad" in one. During the first 12 months the bacterial index improved, as occurs also with dapsone or Ciba-1906, but after that period the further improvement was less than with these two drugs. After 22 months 12 of the cases showed clinical deterioration, and relapses occurred between 14 and 36 months. It is concluded that vadrine has advantages during the first 12 to 18 months on account of its lack of toxicity and side-effects and its rapid therapeutic action. After that period, however, it should be supplemented or replaced by sulphones. The optimum dose is 30 to 40 mg. per kg. body weight daily. , - F. Hawking

70. Vadrine Combined with Sulphone in the Treatment of Lepromatous Leprosy

W. H. JOPLING and D. S. RIDLEY. Leprosy Review [Leprosy Rev.] 32, 188-190, July, 1961. 1 ref.

At the Jordan Hospital, Earlswood, Surrey, and the Hospital for Tropical Diseases, London, 5 lepromatous patients were treated with "vadrine", the initial dosage being 400 mg. daily gradually increased to 1,600 mg. daily by the 4th week and then to 2,000 mg. daily; these doses were accompanied by the standard course of dapsone throughout. During the first 6 months all 5 patients showed excellent clinical improvement; in this period the skin lesions became insignificant, while in the subsequent 6 months they disappeared entirely. Erythema nodosum developed in 3 patients, necessitating interruption of treatment in one case after 6 months and in the other 2 after 12 months. The bacteriological index during, 12 months improved more than it would have done on sulphone alone (except in one of the cases in which treatment had to be interrupted on account of erythema nodosum). On the basis of this admittedly.

small number of cases it is concluded that the combination of vadrine with sulphone is superior to sulphone alone for the early treatment of lepromatous leprosy. There were no toxic effects.

F. Hawking

71. The Treatment of Lepromatous Leprosy with Neovadrine and Vadrine in Combination with DDS J. A. ALIAN. Leprosy Review [Leprosy Rev.] 32, 191-

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193, July, 1961. 1 ref.

"Neovadrine" is the base (2-pyridyl-(4)-1:3:4-oxydiazolone) of which "vadrine" is the p-aminosalicylate At the Ngomahuru Leprosy Hospital, Southern Rhodesia, 10 patients with lepromatous leprosy were treated with neovadrine plus dapsone and 11 with vadrine plus dapsone, the latter in a dosage of 100 mg. daily and vadrine and neovadrine in doses of 200 mg. daily increasing to a maximum of 40 and 20 mg. per kg. body weight respectively. The clinical appearances after 21 months suggested that the response was slightly better than that to dapsone alone. The "biopsy index" fell by 41% in 6 months (but no comparison with cases treated with dapsone alone was available). In 4 cases bacteriological deterioration occurred after 12 months, suggesting the emergence of resistant bacilli. The compounds showed no toxic effects. It is concluded that these compounds accelerate slightly the arrest of the disease compared with dapsone alone, but this acceleration is short-lived and hardly warrants their routine use. F. Hawking

72. The Multipuncture Depot Lepromin Test: I. Technique and Advantages. II. Application to the Study of BCG-induced Lepromin Reactivity

J. A. K. Brown and M. M. STONE. International Journal of Leprosy [Int. J. Leprosy] 29, 1-13, Jan.-March [received Sept.], 1961. 7 figs., 27 refs.

Because of the diminishing availability of lepromin, authors devised a modification of the lepromin testmultipuncture depot lepromin test. As carried of Kumi Ongino Leprosarium, Uganda, the technique to grind 1 g. of autoclaved lepromatous tissue with 1 of a depot medium consisting of light liquid par (15 parts) plus anhydrous lanolin (1 part) together 4 ml. of normal saline, a trace of phenol being adde preservative. A drop of this was placed on the skin 6 punctures were made through it with the Heaf mu puncture apparatus. After about 7 days a late reaction develops at the puncture site in lepromin-positive persons, indicated by 4 or more discrete papules. This reaction is given only to lepromatous material and not to extracts of normal or of tuberculoid skin. It is considered that this test has many advantages, being reliable, economical of antigen, and acceptable to patients.

A test was then performed on 851 children who were given either one lepromin test only, or Heaf tuberculin and depot lepromin simultaneously, or the Heaf tubercu-

lin test 5 weeks earlier; this showed that 55 to 59% of them were lepromin-positive, with no significant difference between the subgroups. In another group of 316° children who were tested with tuberculin (the Heaf or Mantoux test) 82 were shown to be tuberculin-positive and 234 tuberculin-negative. After B.C.G. vaccination of the negative reactors all but 3 became tuberculinpositive and all but 41 became lepromin-positive. The normal lepromin reactor rates increased from 29% at age 5 to 6 years to 78% at age 15 to 16, while after B.C.G. vaccination the rate rose to 86%. With the standard lepromin test 59% of children gave a positive response, but with lepromin diluted to 1:1,000 only 45% gave a positive response. It is considered that the dilute antigen was sufficient to distinguish between those who would give a satisfactory response to normal lepromin and those who would give an unsatisfactory or negative response. It is suggested that conversion to a leprominpositive reaction does not result from the first lepromin test, but from B.C.G. vaccination.

[Those interested should consult the original for fuller details which cannot be included in an abstract.]

F. Hawking

73. The Late Lepromin Reaction in Subsided Lepromatous Cases

N. MUKERJEE and S. KUNDU. International Journal of Leprosy [Int. J. Leprosy] 29, 14-19, Jan.-March [received Sept.], 1961. 4 figs., 9 refs.

In this study, reported from the School of Tropical Medicine, Calcutta, 17 patients with lepromatous leprosy who had been under sulphone treatment for 2 to 9 years and had been clinically and bacterially negative for 2 to 4 years were tested with Mitsuda-Hayashi lepromin to ascertain if any of them had become lepromin-positive after this prolonged and effective treatment. No early reaction was seen in any case, while the late reactions were negative in 15, doubtful in one, and weakly positive in one.

Histological specimens obtained after 3 weeks from the site of lepromin injection gave negative results in 14 cases and a positive result in 3 (one frankly lepromatous case, one atypical lepromatous case, and one borderline). Somewhat similar results had been obtained when these patients were tested at the beginning of their treatment. It is therefore concluded that these results do not confirm reports by other workers that lepromatous patients who have been treated with sulphones often become lepromin-positive.

F. Hawking

74. A New Remedy for Leprosy, Hydroxyprocainepenicillin

R. TRAPPMANN. International Journal of Leprosy [Int. J. Leprosy] 29, 46-55, Jan.-March [received Sept.], 1961. 10 refs.

This report from the Leprosy Research Institute, Djakarta, Indonesia, describes a trial of hydroxyprocaine-penicillin (a combination of benzylpenicillin and the salt hydroxyprocaine, which is derived from paraminosalicylic acid (PAS)) in the treatment of 25 patients over a period of 9 to 12 months, of whom 19 had lepro-

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matous leprosy and 10 were borderline cases; 9 of them had received treatment with sulphones for less than 3 months. The dose was 400,000 units given by intramuscular injection daily.

or of the 19 lepromatous patients one showed marked improvement, 12 some improvement, and 6 no change; of the 12 showing some improvement, there was a decrease in the number of bacilli in 8 but no decrease in the other 4. In 5 patients erythema nodosum developed between the 6th and 8th months, and one suffered from increasing anaemia with enlargement of the liver and spleen after 6 months. However, all the borderline cases responded favourably, 7 of them markedly, and 9 became bacteriologically negative. In 4 patients there was a short reactivation of lesions after 5 to 6 months, and 2 patients developed symptoms of polyneuritis. The lepromin reaction became positive in 4 cases and weakly positive in 4 more.

It is considered that these results are as good as those obtained with sulphone over a longer period and that on the whole the drug is well tolerated. Admittedly the daily injections are a disadvantage and it is recommended that further investigations should be made, especially as to the possibility of giving the drug by weekly injection.

F. Hawkhay

75. Pathology and Bacteriology—Amebiasis. [Review Article]

A. C. Guha. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 362-373, Sept., 1961. Bibliography.

76. Trichlorophenol Piperazine Salt in the Treatment of Intestinal Helminthic Infections in Ethiopia

E. D. WAGNER. American Journal of Tropical Medicine and Hygiene [Amer. J. trop/ Med. Hyg.] 10, 521-522, July, 1961. 1 ref.

The piperazine salt of trichlorophenol contains 80% of 2:4:5-trichlorophenol, which is itself an anthelmintic. The drug was given at the Empress Zauditu Memorial Hospital, Addis Ababa, in the treatment of infections due to Ascaris, Strongyloides, Trichuris, Hymenolepis, and hookworms [species not stated], being administered orally in sugar-coated tablets in single or repeated doses for 1 to 5 days. Direct smears of stools were examined, and for follow-up stool examinations a formalin-ether concentration technique was used. Altogether 53 subjects, mostly Ethiopians (85 worm infections) were treated. A dosage of 1 g. of the drug 3 times daily for 3 or 4 days was considered adequate to remove roundworms and hookworms. The drug had no effect on Trichuris or Hymenolepis nana but had some action on Strongyloides. The reduction in egg-count was not estimated. It is stated that trichlorophenol piperazine salt was less effective than pyrvinium pamoate against threadworms [but no details of the methods used or of the results observed are given].

[The size and frequency of dosage were very variable and the number of patients on each regimen was very small. The total proportion of cures recorded for each worm infection is meaningless because most of the failures occurred with the lower doses.]

L. G. Goodwin

Nutrition and Metabolism

77. Nutritive Value of Bread Made from Flour Treated with Chlorine Dioxide

S. G. IMPEY and T. MOORE. British Medical Journal [Brit. med. J.] 2, 553-556, Aug. 26, 1961. 1 fig., 13 refs.

Previous work has shown that the treatment of flour for bread with chlorine dioxide at levels far in excess of those used commercially in Britain has no toxic effects on animals or human beings cating substantial amounts of such bread for periods up to 22 weeks. The experiments described in this paper from the Dunn Nutritional Laboratory, University of Cambridge, and the Medical Research Council were undertaken to determine whether this treatment of flour would affect the growth of rats in multi-generations. The diet contained 80% by-weight of bread-crumbs made from (a) untreated flour, or (b) flour treated with chlorine dioxide at 30 p.p.m., or (c) flour treated at 300 p.p.m. It was "normalized" by appropriate additions of casein, fat, salts, and vitamins, including vitamin E, and given ad libitum. Equal numbers of male and female rats were allocated to each of the three groups, the same procedure being followed for four generations and the weights of the animals recorded regularly. For both sexes growth was most rapid in the groups given untreated flour, slower in the groups given flour lightly treated with chlorine dioxide, and still slower in the groups given heavily treated flour. These differences were more manifest in the fourth generation. Treatment with chlorine dioxide apparently improved the palatability of the breadcrumbs. H. E. Magee

78. Contribution to the Study of the Steatorrhoeas. (Contribution à l'étude des stéatorrhées). I. Review of the Methods. (I. Critique des méthodes)

H. SARLES, N. PLANCHE, J. N. GOUX, and C. GREUSARD. II. A Study of the Correlations between the Faecal Excretion of Fats and Lipase Activity of Pancreatic Juice. (II. Étude des corrélations entre l'excrétion fécale des graisses et l'activité lipasique du suc pancréatique)

H. SARLES, N. PLANCHE, J. N. GOUX, G. MARCOULIDES, and C. GREUSARD. *Nutritio et Dieta* [*Nutr. et Dieta*] 3, 105-112 and 113-117, 1961. 1 fig., 10 refs.

Most authors have considered that the relation between the amount of fat ingested and the amount excreted in the faeces is a linear one, but recently this view has been questioned. At the Hôpital La Timone, Marseilles, the present authors have studied the problem in 3 subjects, one normal, one with dyspepsia and diarrhoea without any apparent gastro-intestinal lesion, and one with steatorrhoea which was controlled by cortisone therapy. These subjects were given diets containing respectively 5, 15, 30, 60, and 120 g. of fat daily during periods of 5 days on each diet, each study period being started from the day after ingested charcoal appeared in the faeces. The faecal excretion of fat was approximately 1 g. daily when the fat intake was 5 g. daily, and increased proportionately when the fat intake was raised

to 15 g. daily and again to 30 g. daily. With an intake of 60 g. daily, however, the faecal fat excretion showed no further increase and indeed tended to decrease; when the intake was raised to 120 g. daily the level of excretion tended to increase again. The curves obtained varied in respect of the different subjects and in view of the small number could not be analysed mathematically. It is considered, however, that the results support the view that there is no linear relation between the amount of fat ingested and the amount excreted in the faeces.

The authors therefore proceeded to study the excretion of fat in 23 normal subjects receiving an ad libitum diet for periods of 3 to 4 days. It was found that in these subjects the faecal excretion of fat averaged 2.67 ± 0.2 g. daily. Analysis of the results led to the conclusion that a faecal excretion of fat above the level of 5.94 g. day can be considered as definite evidence of steatorrhoea. Further studies showed that in the normal individual receiving an uncontrolled diet it is difficult to obtain an accurate average value for faecal fat excretion even over a study period of 10 days owing to the considerable physiological variations. In pathological conditions where there is considerable abnormality, however, a study period of 3 to 4 days is considered adequate.

In the second study the authors have investigated the correlation between faecal fat excretion and the lipase

content of the pancreatic juice.

In determining the latter a duodenal catheter was kept in the duodenum for 100 minutes, without injection of secretin, and a fraction of duodenal contents drawn off every 10 minutes until 10 fractions had been obtained. Each fraction was then tested for its lipolytic effect on olive oil, the highest value for activity obtained being taken for the purpose of the study. The normal activity of lipase in the pancreatic juice has been found to vary between 35 and 75 units. The 18 subjects studied, who included both normal subjects and patients with chronic pancreatitis [though the number of each is not stated] were given (1) a low-lat diet containing 3 to 7 g. of fat daily, and (2) a diet containing 60 to 70 g. of fat daily, each for 3 to 4 days.

It was found that when the level of lipase activity was below 15 units steatorrhoea resulted from both diets. When the level was approximately 15 units fat excretion was normal, but an increase in lipase activity above this level was not accompanied by a further reduction in faecal fat excretion. It was noted that patients with severe pancreatic deficiency, even when receiving the diet containing only 3 to 7 g. of fat daily, excreted as much as 8 to 10 g. daily in the faeces, indicating that the pancreatic lipase normally acts not only on the ingested fat, but is also concerned in the reabsorption of the fat secreted by the intestine. It is concluded that the findings show a definite correlation between the faecal excretion of fat and the lipase activity of the pancreatic Joseph Parness juice.

Gastroenterology

79. Chronic Chlorpromazine Jaundice: with Particular Reference to Its Relationship to Primary Billiary Cirrhosis A. E. Read, C. V. Harrison, and S. Sherlock. *American Journal of Medicine [Amer. J. Med.]* 31, 249–258, Aug., 1961. 8 figs., 38 refs.

Four patients with chronic chlorpromazine jaundice are described, the icterus lasting 7 to 36 months. The clinical picture was that of prolonged obstructive jaundice with steatorrhoea and weight loss. Three patients showed xanthomatosis. The biochemical changes included very high serum cholesterol and alkaline phosphatase values commencing early in the illness. The clinical picture may resemble that of primary biliary citrhosis but the onset is more acute and a history of receiving the offending drug can be elicited.

In contrast to primary biliary cirrhosis, which is inevitably fatal, clinical recovery ensued in all 4 patients. Elevated serum alkaline phosphatase and cholesterol levels remained for many months after the jaundice had cleared. The histologic picture in the liver resembles that of primary biliary cirrhosis only in the later stages when clinical recovery is in progress. The portal zone infiltration and evidence of liver cell damage are always less in chronic chlorpromazine jaundice than in primary biliary cirrhosis. Although some changes persisted in the liver after clinical recovery, progression to the histologic picture of biliary cirrhosis was not seen.—[Authors' summary.]

80. Intravenous Albumin in the Treatment of Diureticresistant Ascites in Portal Cirrhosis

M. S. Losowsky and M. Atkinson. *Lancet* [Lancet] 2, 386–389, Aug. 19, 1961. 4 figs., 14 refs.

The effect of a course of intravenous infusions of albumin was studied in 10 patients suffering from portal cirrhosis and progressive ascites. Apart from a single case of progressive hepatitis the aetiology of the disease was unknown. Ascites had been present for 3 months to 8 years. Nine of the patients were known to be refractory to dietary sodium restriction and diuretic therapy, while the remaining patient had had no treatment. During the investigation the patients were kept in hospital and given a diet containing approximately 22 mEq. of sodium daily.

After a control period a course of intravenous infusions of salt-poor human albumin was given in a dosage of 50 g. in a litre of pyrogen-free water on alternate days to a total of 150 to 300 g. Of the 7 patients who showed a satisfactory clinical response, 2 died of progressive liver failure 4 and 5 weeks respectively after completion of therapy. The other 5 patients received maintenance therapy with diuretics. Two of these patients have remained free from ascites for 6 and 15 months respectively after cessation of albumin therapy, but in 3 cases ascites re-accumulated after 3 to 4 months; in one of the

latter a further course of albumin therapy was without effect. Thus 4 of the courses of albumin therapy were without effect and in 2 cases the re-accumulation of ascites was hastened. In 2 cases the albumin rendered the patients responsive to diuretic therapy, whereas previously they were refractory. Before treatment the plasma colloid osmotic pressure was subnormal in nearly all patients. Treatment produced a rise in pressure, though this was not significantly greater in the patients who gave a satisfactory response. Colloid osmotic pressure also rose in the ascitic fluid, and it did not appear that the clinical response to albumin could be explained simply on the alteration of the osmotic-pressure gradient between plasma and osmotic fluid. On 6 occasions intrasplenic pressure also increased, the increase being greatest in patients with a high initial pressure. Clinical side-effects of albumin therapy were not pronounced.

W. H. Horner Andrews

81. Contribution to the Problem of Haemorrhage in Cirrhosis of the Liver. [In English]

V. Jirásek and O. Gregor. Gastroenterologia [Gastro-enterologia (Basel)] 96, 1-11, 1961. 3 figs., bibliography.

The part played by coincident peptic ulcer in the aetiology of haemorrhage in cirrhosis of the liver has been studied at the Medical Faculty, Charles University, Prague. In 144 cases in which cirrhosis of the liver was confirmed at necropsy the incidence of peptic ulceration was 11.1% and in 130 cases in which cirrhosis was diagnosed clinically it was 6.9%. A review of the literature showed that while the reported incidence ranged from 1.5% to 24.7%, the majority of workers had obtained figures similar to those in the present series. In contrast the average incidence of peptic ulceration in the general population has been estimated to be about 4%. Haemorrhage from the upper part of the digestive system was the cause of death in one-quarter of the cirrhotics in the present series, and of these, 14% bled not from oesophageal varices, but from a peptic ulcer or a gastric erosion.

To assist in the differential diagnosis of haemorrhage in cirrhosis the urinary uropepsin output was estimated in 48 patients with uncomplicated cirrhosis, 21 patients with gastric ulcer, 54 patients with duodenal ulcer, and 100 healthy subjects. It was found that in the cirrhotics the uropepsin output was extremely low (12 units compared with 53.8 units in patients with duodenal ulcer). Uropepsin analyses were also carried out on 12 cirrhotics with haemorrhage from oesophageal varices and 21 with bleeding duodenal ulcer. The results were comparable with those obtained in the cases without haemorrhage.

It is concluded that coincident duodenal ulcer is a significant cause of haemorrhage in patients with cirrhosis and that uropepsin estimations may be useful in the differential diagnosis. [It is unfortunate that it was not possible to include the uropepsin estimations in a group of patients with cirrhosis and haemorrhage from a duodenal ulcer for comparison with the group with haemorrhage from oesophageal varices.]

T. D. Kellock

82. Electroencephalographic Study of Hepatic Encephalopathy. (Étude electroencephalographique de l'encéphalopathie hépatique)

R. CLOCHE. Revue internationale d'hépatologie [Rev. int. Hépat.] 11, 245-269, 1961. 15 figs., 17 refs.

The author has studied at the Hôpital Beaujon, Paris, the electroencephalograms (EEGs) of 25 men and 13 women in various stages of liver failure. Neurologically, the cases ranged from those with slight neurological and psychological disturbance to those in deep coma. The main departures from the normal EEG were a predominant delta rhythm of rather angular shape, but regular in amplitude and frequency, and triphasic delta waves. In patients in precoma or light coma these waves were abolished by opening the eyes or by making a mental effort. The author states that of these two types of change, neither is specific to liver failure, but he has not seen them in other forms of coma—hypoglycaemic. uraemic, or acidotic—of metabolic origin, though similar changes are occasionally seen after head injury. It was noted that the deeper the coma, the more constant the G. S. Crockett

83. Metabolic Epilepsy and Severe Hepatic Insufficiency. (Epilepsie métabolique et insuffisance hépatique grave)

G. BOUDIN, M. CACHIN, and M. NIVET. Revue internationale d'hépatologie [Rev. int. Hépat.] 11, 271-301, 1961. 6 figs., 47 refs.

The authors describe in detail 9 cases of severe liver failure due to alcoholic hepatic cirrhosis. In all cases at least one epileptic seizure occurred during the later stages of the disease. All the patients died and in most cases necropsy and histological examination of the brain were carried out. In most cases the electroencephalogram showed general slowing of activity and in some the presence of theta rhythm with paroxysmal delta anomalies. It is stated in discussion that the epilepsy can be ascribed to no particular cause; several hypotheses are discussed and it is concluded that it is probably a part of the general disorganization of cerebral function which occurs in severe hepatic failure. A photomicrograph shows the histological appearance of the brain in one case in which lesions were found in the left Rolandic region and both temporal lobes.

G. S. Crockett

84. The Treatment of Severe Hepatic Failure with Malic Acid in Association with Arginine. (Le traitement de la grande insuffisance hépatique par l'association acide malique-arginine)

M. CACHIN. Presse médicale [Presse méd.] 69, 1473-1475, July 1, 1961. 5 figs., 21 refs.

L-Arginine has been given to patients in hepatic coma in order to reduce blood ammonium levels, although reports on its therapeutic efficacy have been conflicting. In a quite different connexion malic acid has been shown to protect rats against the hepatotoxic effects of carbon tetrachloride. In the present study, carried out at the Hospice de la Salpêtrière, Paris, the author found that a combination of L-agginine and malic acid gives rats more protection against the lethal effects of an intraperitoneal injection of ammonium carbonate than does arginine alone. He has therefore used this combination of drugs in the treatment of 22 patients with hepatic coma due to cirrhosis of the liver, giving a daily infusion of 750 to 1,250 ml. of a solution containing 17.5 g. of malic acid and 16.8 g. of L-arginine per litre. Recovery was achieved in 16 of 25 episodes of hepatic coma, the blood ammonium level being reduced and abnormal electroencephalograms reverting towards normal.

[The effect of therapy in hepatic coma is notoriously difficult to assess and there is no adequate substitute for properly controlled clinical trials.]

P. C. Reynell

85. Gastrointestinal Protein Loss Demonstrated by ⁵¹Cr-labelled Albumin

T. A. WALDMANN. Lancet [Lancet] 2, 121-123, July 15, 1961. 12 refs.

The author reports from the National Cancer Institute. Bethesda, Maryland, a new method for the detection and assessment of the loss of protein into the intestinal tract which appears to be more reliable than previous methods in which either albumin or polyvinylpyrrolidone labelled. with ¹³¹I was used. The former is rapidly hydrolysed to amino-acids and these and the iodide are quickly reabsorbed, while the latter is not a natural metabolite. It has been shown that radioactive chromium (51Cr) chloride is poorly absorbed from the gut and for this reason 51Cr-labelled erythrocytes have been used for assessing the site and amount of loss of blood in the gut. The same principle is now applied to the loss of protein. The material for injection was prepared by incubating albumin in 10% glucose at pH 4.5 with 51Cr chloride at room temperature for one hour, free chromium being then removed by passage through either "dowex-50" resin or "amberlite" resin; the latter proved the more satisfactory.

When the labelled albumin was given by mouth to 9 patients without gastro-intestinal disease 93 to 98% of the radioactivity was recovered in a subsequent 4-day stool collection. When given intravenously to 15 control patients with hypoproteinaemia but no intestinal disorders only 0.06 to 0.63% of the dose appeared in the faeces in the subsequent 4 days. In contrast, when labelled albumin was given to 8 patients with known gastro-intestinal protein loss 4.2 to 21% appeared in the stools in the same period. In one patient with intestinal lymphangiectasia it was possible to demonstrate radioactivity in the jejunal contents when it was absent from the gastric juice, confirming that the site of the protein loss was the jejunum.

[These findings, taken with the theoretical objections to previous methods mentioned above, suggest that this technique should be more reliable for the assessment and possible location of intestinal protein loss.]

T. D. Kellock

Cardiovascular System

86. Sequelae of Left Ventricular Puncture with Anglocardiography

V. O. BJÖRK, I. CULLHED, A. HALLEN, H. LODIN, and E. MALERS. Circulation [Circulation] 24, 204-212, Aug., 1961. 1 fig., 34 refs.

Since 1958, at the University Hospital, Uppsala, Sweden, left ventricular puncture has been carried out for pressure measurements and injection of contrast material on 142 occasions on 137 patients, and in the present paper the complications encountered are described. In one case the needle caused very frequent ventricular premature beats; in another ventricular fibrillation requiring cardiac resuscitation occurred; while in 2 cases the needle entered the right ventricle. In 5 further cases no injection was possible for technical reasons. Ventricular puncture was successfully performed on 133 occasions.

In most instances no pain or only slight pain was experienced: Ventricular extrasystoles were usual while the needle traversed the ventricular wall. Injection of contrast medium usually caused a few ventricular extrasystoles, a moderate tachycardia, and a fall in blood pressure. A slight rise in temperature was common in the first 24 hours, even in the absence of other complications. Minor complications included left pneumothorax in 8 cases (of the "noisy" type in 2), minimal pleural effusion (usually left-sided) in 15, pulmonary changes in the radiograph in 8, and atrial fibrillation within 48 hours of the procedure in 2. Significant amounts of blood without signs of tamponade were found in the pericardial sac in 4 cases during subsequent operations carried out between the 8th and 30th days. Major complications were cardiac tamponade in 6 cases (2 fatal), and faulty, usually intramyocardial, injection of contrast material in 4 (one fatal). In one patient ventricular fibrillation responded to resuscitative measures and in 2 others there was a temporary cerebral disturhance.

The literature on the complications of ventricular puncture in some 900 cases (8 of which were fatal) is reviewed and practical advice is given for the prevention of cardiac tamponade and intramyocardial deposition of contrast material. In spite of a definite morbidity ventricular puncture remains a useful and practical procedure for the investigation before major heart surgery of patients with aortic stenosis and mitral insufficiency. T. Semple

87. The "Two-step" Exercise Test Brought up to Date

A. M. MASTER and I. ROSENFELD. New York State Journal of Medicine [N.Y. St. J. Med.] 61, 1850-1858, June 1, 1961. 1 fig., 38 refs.

This is a reappraisal from the Mount Sinai and New York Hospitals of the "two-step" exercise test of cardiac function devised by the senior author and its use in

conjunction with electrocardiography for the diagnosis of coronary arterial disease. The test as described in the present paper and elsewhere has been found perfectly safe in 52,000 examinations. The principal danger is the failure to recognize impending myocardial infarction which, of course, is an absolute contraindication. The incidence of pain induced by the test is 6%, but is higher in those with definite organic heart disease. The original criterion of an abnormal result was an RS-T depression of more than 0.5 mm., but more recent work has shown that the configuration of the depression is more important than the depth. The ischaemic RS-T depression must be distinguished from the "junctional" ("j") type or false positive type. Any depression of the segment characterized by an initial horizontal course of at least 0.08 second or by a definite sag is abnormal. A negative response to the double "two-step" test provides an assurance of at least 30 to 1 that the patient has no interference with the coronary supply. If a history of angina conflicts with a negative test result, then the Q-T ratio should be measured. If the actual Q-T time is at least 10% greater than that of normal persons with the same heart rate, then the result should be considered abnormal. An ischaemic depression of the RS-T segment can be regarded in at least 95% of cases as an indication of organic involvement of the heart itself or of its nutrition, even when the depression measures only \(\frac{1}{2} \) mm. or less.

The authors do not consider that a "j" depression always indicates "functional" disease. If this depression is 2 mm. or more it usually indicates coronary insufficiency. If the QX/QT fraction, which is the relation of the duration of the RS-T depression (QX) to the entire electrical systole (QT), is found to be less than 50% this is good evidence that the "j" depression is functional in origin.

T. Semple

88. Practical Clinical Applications of Vectorcardiography G. E. Burch and N. P. Demasquale. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 301–307, Oct. 21, 1961. 13 figs., 11 refs.

89. Pericardial Effusion in Clinically Inactive Compensated Rheumatic Heart Disease

W. L. WINTERS JR. and L. A. SOLOFF. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 173-176, Aug., 1961. 24 refs.

Pericardial effusion is sometimes found unexpectedly at operation in patients with rheumatic heart disease, and in order to assess the incidence of such effusions venous angiography was performed in conjunction with right heart catheterization on 141 patients with chronic rheumatic carditis and 66 with other forms of heart disease. At the time of study, which was carried out at Temple

University Medical Center, Philadelphia, no patient was in congestive failure or had evidence of active carditis. Pericardial effusion was diagnosed by demonstrating a softer homogeneous shadow outside the opacified heart, either surrounding it or confined usually to the lateral border of the right atrium.

An effusion was found in 5 patients (3.5%) all of them females with mitral valve disease and atrial fibrillation. In the past 3 of them had had congestive failure and another had developed hypothyroidism after treatment with radioactive iodine. Normal right atrial and ventricular pressures were recorded on cardiac catheterization in 3 patients, but in 2 the mean right atrial and right ventricular diastolic pressures were slightly raised.

None of the 66 patients with congenital, hypertensive, or coronary arterial disease, on the other hand, was discovered to have a pericardial effusion. The authors suggest that in rheumatic heart disease effusions forming during episodes of active carditis or congestive failure may persist owing to the altered reabsorptive capacity of the pericardium.

90. Persistent Kidney Lesions after Subacute Bacterial Endocarditis. (Über die persistenten Nierenveränderungen nach Endocarditis lenta)

I. SZAM and L. PÖLCZ. Zeitschrift für die gesamte innere Medizin und ihre Grenzgebiete [Z. ges. inn. Med.] 16, 596-599, July 15, 1961. 3 figs., 19 refs.

A follow-up of 80 cases treated at the 4th Medical Clinic of the University of Budapest for subacute bacterial endocarditis complicated by renal lesions showed that 22 of these patients had died of their endocarditis and 11 others could not be traced. The remaining 47 patients, 34 men and 13 women, were studied for periods varying from one to 12 years in order to ascertain whether, although the endocarditis had been successfully treated, the renal lesions too had been cured. Renal function tests were performed at follow-up, while post-mortem material was also examined. The kidneys were judged to be intact in 24 living patients and in 10 who had died from non-renal causes. In 6 living patients microscopic haematuria and albuminuria were present, although renal function test results were normal. Chronic nephritis was found in 7 patients, all males. In 5 of these blood culture gave a positive result, whereas this was the case in only 7 of the other 40 patients, and 5 suffered from aortic incompetence, whereas the aortic valve was affected in only 18 of the other 40. Of the 7 chronic nephritics, one died in heart failure, one in renal failure complicating cardiac decompensation, and one from uraemia. The authors stress that the renal lesions may become chronic even when the subacute bacterial endocarditis has responded to treatment and that such chronic lesions carry a gloomy prognosis. On the other hand a pathological urine, provided renal function is good, is no indication of relapse of septic processes in the kidney. During life no differential diagnosis can be made between diffuse and focal glomerulonephritis. There is no difference in the prognosis of these two conditions, since both may equally readily become chronic. E. S. Wyder

-VALVULAR DISEASES

91. Long-term Course of Patients with a Basal Diastolic Murmur and Predominant Mitral Stenosis M. G. Magida and D. M. Roseman. New England Journal of Medicine [New Engl. J. Med.] 265, 118-120, July 20, 1961. 1 fig., 4 refs.

The authors of this paper from the New York Hospital-Cornell Medical Center review the long-term clinical course in 81 patients with a basal diastolic murmur and mitral stenosis. The patients (46 male and 35 female, average age 33.8 years) had been under observation in the same clinic since childhood. They were divided into three groups: (1) those in whom the basal diastolic murmur was accompanied by peripheral evidence of aortic regurgitation; (2) those with a normal pulse pressure, the criterion being that this pressure should not exceed 60 mm. Hg and that the diastolic pressure should not fall below 50 mm. Hg, and (3) those in whom a basal diastolic murmur had now regressed. The patients were also divided into Grades 1 to 4 of increasing disability.

The average duration of the basal murmur was 17 years and all except 7 of the patients were free from. symptoms for an average of 15 years after the appearance of the murmur. In 39 patients symptoms referable to the heart or lungs developed but did not progress for an average period of 2.7 years in those in the highest grade of functional ability. The average interval before death once symptoms developed, however, was only 2 years for the whole series. There were 35 deaths, 34 being in Groups 1 and 2, with a roughly equal distribution between the two groups. In 9 of the 34 patients death was due to active rheumatic carditis and in 5 to subacute bacterial endocarditis; 7 patients died suddenly and 13 died from intractable cardiac failure. No difference was demonstrated before the onset of symptoms between those who survived and those who died.

The authors consider that with the improved treatment of cardiac failure and the availability of antibiotics and corticosteroids many of these deaths can now be prevented. They emphasize, however, that in patients with mitral stenosis the presence of a basal diastolic murmur fulfilling the criteria of a Graham Steell murmur does not preclude aortic regurgitation. The classic signs of associated peripheral vascular dynamics are not, in their view, essential for the diagnosis, and pulmonary regurgitation is probably rare; this should be taken into account when surgical intervention is considered.

J. Warwick Buckler

92. Retrograde Catheterization of the Left Ventricle and Angiography in the Diagnosis of Mitral-valve Disease O. E. Starobin, D. Littmann, C. A. Sanders, and J. D. Turner. New England Journal of Medicine [New Engl. J. Med.] 265, 462-468, Sept. 7, 1961. 5 figs., 13 refs.

In this communication from Harvard Medical School, Boston, the authors consider the value of percutaneous retrograde arterial catheterization of the left ventricle in the assessment of patients for surgery of the mitral valve. They have studied 53 patients by a modified Seldinger

technique, involving percutaneous puncture of the pressure was low, particularly where the mitral incomfemoral artery and passage of a catheter into the left ventricle for the recording of pressures and injection of contrast medium. The amount of mitral regurgitation present was assessed from the degree of opacification of the left atrium in angiograms after injection of contrast medium into the left ventricle, and the pressure gradient across the mitral valve was estimated from the difference in diastole between the left ventricular pressure and the pulmonary capillary pressure simultaneously measured by right heart catheterization.

In 21 patients with clinical mitral valvular disease adequate data were obtained and these were compared with the surgeon's subsequent findings at operation. This revealed an excellent correlation, the findings by both methods agreeing in completely separating a group of 11 patients with little or no regurgitation from 10 with significant to severe regurgitation. In 7 patients the clinical assessment was misleading and angiocardiography was critical in making the correct diagnosis. In particular, in 5 of 7 patients thought clinically to have both significant stenosis and regurgitation angiocardiography correctly excluded important incompetence of the valve and allowed the surgeon to perform a closed valvotomy instead of using the more hazardous open-heart approach.

Simultaneous right heart and left ventricular catheterization enabled the pressure gradient at the mitral valve to be measured and à calculation made of the estimated mitral valve area. When this estimate was compared with the findings at surgery excellent agreement was found in 8 cases in which there was no significant degree of regurgitation. In 5 cases with important regurgitation the preoperative estimate of the mitral valve area was too small, but could be corrected when allowance was made for the amount of incompetence as determined by angiography. The authors conclude that the technique described is reasonably safe, causes few complications, and can provide important information which may be helpful in the selection of patients for mitral valvotomy. M. Harington

93. Syndrome of Mitral Incompetence, Myocarditis, and Pulmonary Hypertension in Nigeria

D. ABRAHAMS and W. BRIGDEN. British Medical Journal [Brit. med. J.] 2, 134-139, July 15, 1961: 10 figs., 24 refs.

This paper from University College Hospital, Ibadan, describes 50 patients, observed over a relatively short period in the western region of Nigeria, who presented with congestive cardiac failure due to mitral incompetence and pulmonary hypertension and were admitted to hospital for treatment and investigation. Threequarters of them were under 30 years of age, and wemen were affected twice as often as men. The main symptoms were substernal cardiac pain and effort dyspnoea; orthopnoea was notably absent. Oedema of the legs and ascites were present in half the cases, together with physical signs of mitral incompetence and pulmónary hypertension.

The patients were all in sinus rhythm with one exception, although ventricular extrasystoles were common. A low systemic arterial pressure was usual and the pulse

petence was severe. The degree of left ventricular hypertrophy was such that the left chest was deformed in the younger patients. There was no evidence of aortic valve disease, and mitral diastolic murmurs were heard only in those patients in whom active carditis was thought to be present.

Cardiac catheterization confirmed the high pulmonary arterial pressures and the low cardiac output. All patients had anaemia, and this was of an iron-deficiency type refractory to oral therapy. Necropsy was performed on 13 patients, and the presence of left ventricular myopathy and mitral valvulitis together with a macroscopic endomyocardial fibrosis was confirmed. The inflammatory reaction was of a diffuse, non-specific type, although some patients showed Aschoff nodules indistinguishable from those found in rheumatic carditis. In 6 cases the antistreptolysin-O titre as determined before death was found to be raised. Histological examination of the heart in these 6 cases showed typical Aschoff nodules and non-specific myocarditis.

The authors emphasize that in the district from which their patients were drawn anaemia, intestinal parasitism, malaria, dysentery, and malnutrition are usual, and that this persistent chronic ill-health combined with continued physical activity may in itself lead to cardiomyopathy, thereby rendering the myocardium relatively more vulnerable to rheumatic carditis than the endothelium of the valves or the joint tissues. J. Warwick Buckler

.94. Mitral Valvotomy: a Comparison of Results by Two Operative Methods

K. FRASER and I. F. KERR. British Medical Journal [Brit. med. J.] 2, 339-342, Aug. 5, 1961. 15 refs.

The authors have reviewed the records of 221 patients subjected to mitral valvotomy at the Western Infirmary, Glasgow, during the period 1951-60, all the operations having been performed by the same surgeon (the firstnamed author). For comparative purposes they were divided into two groups: (1) in the first 150 patients valvotomy was performed through the left atrial appendage by the finger or in some cases the finger and a Brock knife; (2) in the remaining 71 patients treated after August, 1957, valvotomy was by the transventricular route, using Tubbs's expanding dilator. It is interesting to note that the presence of an "opening snap" was not always necessarily indicative of a mobile valve. The, use of a dilator ensured a better split of the valve, an opening of 3.5 cm. or more being obtained in 98.6% of the "dilator group" compared with only 16.6% of the "finger-knife group". The incidence of postoperative mitral regurgitation was greater following the use of the dilator (32% compared with 24%), though in most cases such regurgitation was only slight and usually took place at the posterior commissure; the incidence of moderate or severe incompetence of the valve was the same in both groups. Calcification was present in 38% of all cases, but did not prevent a satisfactory split in those in which the dilator was used.

The operative mortality was lower in the dilator group. (5 deaths) than in the finger-knife group (14); death due

to embolus occurred 5 times in the latter group compared during operation. There were 3 deaths in the series, one deaths, all of patients in Group 1. Of the 187 survivors, 185 were available for follow-up. The preoperative mitral diastolic murmur disappeared in 67:2% of the cases in which the final valve opening was more than 4. cm., but in only 10.9% of those in which the final opening was less than 4 cm. The authors conclude: "Although it is perhaps early to be certain of the late results in cases where the dilator has been used, it is encouraging that, so far, all survivors from this operation are in the good 'to 'excellent' category." The effect of auricular fibrillation on operative mortality and prognosis is discussed. R. L. Hurt

95. Correction of Aortic Regurgitation Using Plastic

E. B. KAY, D. MENDELSOHN JR., A SUZUKI, and H. ZIMMERMAN. Journal of the American Medical Association [J. Amer. med. Ass.] 176, 1077-1081; July 1, 1961.

The three main factors in successful surgery of the aortic valve have been (1) the development of surgical techniques ensuring optimum correction and function of the valve, (2) a procedure providing adequate protection of the myocardium which allows ample time for surgical correction, and (3) proper selection of patients before irreversible left ventricular failure occurs. Therefore in patients with aortic insufficiency operative treatment should be advised for those in whom the heart is significantly large, or is enlarging, and before the onset of cardiac failure.

From St. Vincent Charity Hospital, Cleveland, Ohio, the authors report 22 cases in which aortic regurgitation was surgically corrected by means of an artificial plastic valve shaped like the normal valve. In 19 of these cases polytetrafluoroethylene, ("teflon") fabric was the material of choice, while in the other 3 compressed polyvinyl formol ("ivalon") sponge was used. Two types of procedure were employed: where the valve was extensively calcified and stenosed it was excised completely and the artificial valve was attached to the aortic annulus through a buttress formed by a 2-mm, strip of teflon felt covered with teflon fabric; in other cases the artificial valve was sutured to the remaining leaflet tissue.

Operation was performed with the aid of a by-pass technique, using general hypothermia (24 to 28° C.) in conjunction with selective cardiac perfusion of hypothermic blood (at 20 to 24° C.) at a rate of 200 to 350. ml. per minute. For the initial 10 to 15 minutes necessary for aortic incision and coronary cannulation cardiac arrest was produced by coronary perfusion of oxygenated ice-cold Ringer's solution through a cannula inserted in the base of the cross-clamped aorta. Subsequently, as hypothermic blood was perfused through the coronary vessels and the myocardial temperature slowly rose, fibrillation returned. This was allowed to continue until the end of the operation when, after rewarming the heart to 30 to 34° C., the normal beat was restored by electrical defibrillation. The authors believe that this technique provides the maximum degree of myocardial protection

with only once in the dilator series. There were 15 late at 24 hours from a haemorrhagic diathesis involving the small intestine and 2 from bacterial endocarditis at 8 and 10 weeks after operation. The remaining 19 patients were entirely well one year after operation (one after re-operation for recurrent aortic incompetence), all having a normally functioning aortic valve.

F. J. Sambrook Gowar

96. The Graham Steell Murmur versus Aortic Regurgitation in Rheumatic Heart Disease: Results of Aortic Valvulography

V. RUNCO, W. MOLNAR, C. V. MECKSTROTH, and J. M. RYAN. American Journal of Medicine [Amer. J. Med.] 31, 71-80, July [received Sept.], 1961. 6 figs., 33 refs.

From Ohio State University Hospital, Columbus, Ohio, the authors report their experience with retrograde aortic valvulography which is of value in enabling the important differentiation to be made between relative pulmonary insufficiency and aortic regurgitation in patients with rheumatic heart disease. The method consists in delivering into the aorta 10 to 15 ml. of concentrated iodine contrast medium during each of four successive cardiac cycles by means of a catheter, the tip of which is sited at the level of the aortic sinuses. The amount of reflux of contrast medium into the left ventricle observed in serial radiographs (4 to 6 frames per second) taken during diastole is graded into four degrees of severity, ranging from slight regurgitation clearing during the next systole to complete outlining of the left ventricle.

There were no complications due to this method in any of the 25 patients studied, who were divided into two groups: (1) 13 patients with clinical evidence of mitral. stenosis in whom a basal diastolic murmur thought to be a Graham Steell murmur was heard, 4 of this group being also thought to have mitral regurgitation; and (2) 12 patients in whom no definite origin for the basal diastolic murmur could be defined on clinical grounds. usually because of the coexistence of mitral regurgitation. Retrograde aortic valvulography showed that of the 13 patients in Group 1, 10 had aortic regurgitation, a finding that could not have been detected clinically. Moreover, in the 3 without regurgitation exactly similar physicalsigns were present as in the rest of the group. Of the 12 patients in Group 2, 8 had a ortic regurgitation, and again there was no clinical means of arriving at this finding; in 4 of these cases in which there was left ventricular hypertrophy mitral incompetence could have been the cause.

Discussing these results the authors point out that in the past erroneous clinical evaluation has led to disappointing results after surgery, particularly in cases in which mitral regurgitation and lesions of the aortic valve coexist. They suggest that relative pulmonary insufficiency is diagnosed too frequently, partly because it is often indistinguishable clinically from aortic regurgitation. This may be the explanation of some of the failures of surgery, for they have noted that in patients with the more severe grades of aortic regurgitation demonstrated by the method described mitral commissurotomy has not been successful. So far no reliable method of detecting pulmonary valvular incompetence has been found, but as this study shows that the majority of patients thought to have a Graham Steell murmur have in fact unsuspected aortic regurgitation it is suggested that aortic valvulography should be performed on all patients who are being prepared for commissurotomy and who have a basal diastolic murmur.

J. S. Malpas

DISTURBANCES OF RHYTHM AND CONDUCTION

97. Calcium, Chelates, and Digitalis: a Clinical Study R. S. ELIOT and S. G. BLOUNT JR. American Heart Journal [Amer. Heart J.] 62, 7-21, July, 1961. 5 figs., 15 refs.

Calcium increases and mimics the action of digitalis in many ways, including the production of arrhythmias. Thus a reduction in the level of ionized calcium in the blood should reduce the effect of digitalis. The intravenous injection of the chelating agent trisodium ethylenediamine tetraacetate (Na₃ EDTA) is one of the best ways of obtaining a rapid, transient hypocalcaemia.

This paper from the University of Colorado Medical Center, Denver, describes the use of Na₃ EDTA in 63 patients, of whom 35 had signs of digitalis overdosage, 16 had cardiac arrhythmias unrelated to digitalis, and 12 had no cardiac abnormality. The drug was given by intravenous injection (usually 3 to 4 g. of Na₃ EDTA in 250 ml. of 5% glucose in water) over 12 minutes. This treatment was effective in reversing arrhythmias, temporarily or permanently, in most of the patients with digitalis intoxication, but was more unreliable in nondigitalized patients. The subjective symptoms of digitalis intoxication were relieved during the injection in all affected patients and the effect preceded the electrocardiographic changes. Toxic effects of the injection included arm pain, circumoral paraesthesiae, and apprehension. The injection can be used as a test to predict the beneficial effect of digitalis withdrawal combined with oral potassium chloride. T. Semple

98. A-V Nodal Tachycardia with Block

A. PICK, R. LANGENDORF, and L. N. KATZ. Circulation [Circulation] 24, 12-22, July, 1961. 7 figs., 47 refs.

Paroxysmal as well as nonparoxysmal varieties of rapid ectopic rhythms originating in the A-V node may be associated with various conduction disorders involving propagation of regularly generated impulses to the atria and ventricles as well as within the ventricles. This may occur following treatment of a paroxysmal tachycardia by digitalis or when impulse formation within the node becomes accelerated as a consequence of digitalis excess.

Since retrograde and forward conduction may vary independently and since the tachycardia frequently develops in the presence of atrial fibrillation, actual conduction times through the A-V junction may not be measurable. The nature of the arrhythmia must be diagnosed from the spacing and characteristic grouping of ventricular or atrial complexes or from changes in the configuration of the ventricular beats.

Several varieties of such nodal tachycardias with block are presented, including examples of (a) A-V dissociation in atrial fibrillation with Wenckebach periods of forward conduction; (b) A-V dissociation during sinus rhythm with Wenckebach periods of antegrade nodal impulses; (c) Wenckebach periods of forward conduction with constant retrograde conduction; (d) Wenckebach periods of both forward and retrograde conduction, with blocked re-entry as a possible mechanism of intermittence of the tachycardia; (e) complete and incomplete A-V dissociation due to acceleration of two nodal pacemakers; and (f) aberrant ventricular conduction simulating ventricular premature beats or resulting in a bi-directional type of tachycardia.—[Authors' summary.]

99. A Histopathologic Study of the Atrioventricular Communications in Two Hearts with the Wolff-Parkinson-White Syndrome

M. LEV, R. KENNAMER, M. PRINZMETAL, and Q. H. DE MESQUITA. Circulation [Circulation] 24, 41-50, July, 1961. 14 figs., 27 refs.

Knowledge of the anatomical basis of accelerated atrio-ventricular (A-V) conduction is still fragmentary since, as the authors point out, very few hearts from patients suffering from the Wolff-Parkinson-White syndrome have been investigated histologically. They have therefore studied extensively serial sections of the hearts of 2 such patients seen at the Matarazzo Hospital, São Paulo, Brazil. In one case the approaches to the A-V node showed heavy lymphocytic infiltration and degenerative changes in the A-V bundle, while in the other there was moderate fibroelastosis near to and at the A-V node and moderate infiltration of the bundle with mononuclear cells. The first patient had had definite Chagas's myocarditis and this was probably also present in the second. In one case there was muscular communication between the right atrium and right ventricle and in the other the right bundle branch was abnormal.

In a review of the available literature the authors found that in 3 of the 4 reported cases which had been minutely studied there were abnormal muscular communications between the atria and the ventricles and in other cases a high incidence of inflammatory changes in the bundles. They conclude that further detailed study is required.

J. R. Belcher

100. Adrenocortical Steroids in Intermittent Heart-

B. W. PAY and VISCOUNT WAVERLEY. British Medical Journal [Brit. med. J.] 2, 139-142, July 15, 1961. 6 refs.

This paper from the Royal Berkshire Hospital, Reading, presents the case histories of 6 patients with heart block and subsequent Stokes-Adams attacks which hadfailed to respond to conventional therapy. These patients were given prednisolone, usually starting with 80 mg. daily by mouth, and in all of them the attacks stopped within 48 hours and have not recurred. The dose used for maintenance treatment has been from 10 to 15 mg. daily, although as much as 60 mg. has been given by other authors. There have been no untoward effects from this treatment.

The value of corticosteroid therapy in these cases is stressed by the authors. They consider it to be of special value in patients with an unstable atrioventricular block, but that it is less likely to restore normal rhythm when complete heart block is established. Where syncope is accompanied by ventricular standstill, however, some relief may still result.

J. Warwick Buckler

CORONARY DISEASE AND MYOCARDIAL INFARCTION

101. Serum Creatine Kinase in the Diagnosis of Myocardial Lesions. (La créatine-kinase sérique dans le diagnostic des lésions myocardiques)

L. SCEBAT, J. RENAIS, and J. LENÈGRE. Archives des maladies du cœur et des vaisseaux [Arch. Mal. Cœur] 54, 721-731, July, 1961. 5 figs., 5 refs.

This work from the Hôpital Boucicaut, Paris, describes the serum creatine kinase findings in 150 patients, of whom 85 had coronary arterial disease, with myocardial infarction in 56 cases. The normal level was 0 to 1 unit with an average of 0.4 unit. When infarction occurs the level rises above 1.4 unit after 17 hours to an average maximum of 11.3 units at 33 hours, returning to normal after 92 hours. Slight elevations up to 4.4 units were observed in 30% of cases of disturbances of repolarization, but not in cases of angina pectoris. Lesions of skeletal muscle, especially after arterial obstruction, caused elevated serum creatine kinase levels for periods up to 15 days, but there was no rise in cases of cardiac insufficiency of non-coronary origin, pulmonary embolism, haemolytic disease, cerebral thrombosis, or hepatitis.

102. Serum Lipids, Hypertension and Coronary Artery Disease

M. J. Albrink, J. W. Meigs, and E. B. Man. American Journal of Medicine [Amer. J. Med.] 31, 4-23, July [received Sept.], 1961. 7 figs., bibliography.

In a study at the Yale-New Haven Medical Center, New-Haven, Connecticut, serum triglyceride levels were estimated in 115 patients who had had myocardial infarction at least 10 days previously and in 397 apparently healthy controls. A distinctly raised level was found in 82% of all patients with coronary arterial disease, but in only 36% of apparently normal subjects aged 30 and over. The authors state that estimation of serum triglyceride levels "appeared to provide a better separation between normal persons and patients with coronary artery disease than the reported measurements of other serum lipids". They consider that a raised serum cholesterol level is of significance only in relatively young patients with coronary arterial disease and does not offer differential help in patients over 50 years of age. Hypertension and a high serum cholesterol level (over 260 mg. per 100 ml.) appeared to be of little significance by themselves, but definitely increased the risk of coronary arterial disease in patients with a high serum triglyceride level. However, in a limited number of patients under 50 suffering from coronary arterial disease

a high serum cholesterol level, even in the absence of a raised serum triglyceride level, appeared to be characteristic of the disease; but in the large majority of patients with coronary arterial disease at all ages an increased serum triglyceride concentration appeared to be the most significant abnormality. It is emphasized, however, that "a causal relationship of serum lipids to coronary artery disease is unproved".

Z. A. Leitner...

103. Hypercholesteremia and Nicotinic Acid: a Long-term Study

K. G. Berge, R. W. P. Achor, N. A. Christensen, H. L. Mason, and N. W. Barker. *American Journal of Medicine [Amer. J. Med.]* 31, 24-36, July [received Sept.], 1961. 5 figs., bibliography.

In a study at the Mayo Clinic, Rochester, Minnesota, it was found that nicotinic acid in doses of 1.5 to 6 g. daily significantly reduced the serum cholesterol level; increasing the dose increased the rate of reduction. In 80% of 51 patients with hypercholesterolaemia treated for a year or more the serum cholesterol level was reduced from a mean of 327 mg. per 100 ml. initially to 250 mg. per 100 ml., and this decrease was sustained so long as adequate doses of nicotinic acid were given.

In the course of treatment with nicotinic acid of 15 cases of xanthoma tendinosum the xanthomata disappeared in one case and decreased in size in 2 others; xanthelasmata disappeared in one case and decreased in size in 2 cases. No objective evidence of improvement could be found in atherosclerotic heart disease, although subjective improvement was registered in several cases; nevertheless, 11 patients died during or after treatment with nicotinic acid from complications of atherosclerosis.

Side-effects necessitated discontinuing the use of the drug in 8 of 66 cases. Cutaneous flushing, pruritus and mild urticaria with occasional dryness of the skin, gastro-intestinal irritation with anorexia, nausea, vomiting, and diarrhoea were the most frequent side-effects. Impairment of hepatic function with jaundice, which occurred in 2 cases, was a further untoward side-effect.

According to the authors the mechanism of the action of nicotinic acid on the cholesterol level or in causing side-effects is unknown. They consider that its use "in the investigative treatment of hypercholesteremia is warranted and may ultimately provide insight into the possible value of lowering elevated levels of cholesterol in the blood as a means of treatment or prevention of atherosclerosis".

Z. A. Leitner

104. Comparative Effects of Thyroxin Analogues as Hypocholesteremic Agents

M. M. BEST and C. H. DUNCAN. Circulation [Circulation] 24, 58-67, July, 1961. 8 figs., 15 refs.

The administration of thyroid hormones in sufficient quantities reduces an elevated serum cholesterol level in euthyroid subjects, but their use in patients with coronary arterial disease is limited by the fact that they frequently increase the severity of angina pectoris. However, some of the thyroid hormone analogues exert the same beneficial effect on cholesterol metabolism while having a less pronounced influence on oxygen consumption. In this

study, reported from the University of Louisville, Kentucky, four of these analogues, namely, iodothyroformic acid, dimethyldiiodothyroformic acid, D-thyroxine, and D-triiodothyronine, were given to 17 hypercholesterolaemic euthyroid patients, of whom 14 had arteriosclerotic heart disease, for various periods up to 10 months in subgroups of 4 to 9 patients each. The results were compared with those after administration of L-thyroxine.

All the analogues reduced the mean serum cholesterol level, which had been 286 (maximum 394) mg. per 100 ml., without increasing the basal metabolic rate or aggravating the symptoms of angina pectoris. The reduction in the serum cholesterol level was maintained throughout the period of hormone administration, but after the replacement of the analogue by a placebo the level returned to the pre-treatment value. While L-thyroxine also effected a modest sustained reduction in the serum cholesterol level, in the 2 patients with severe angina pectoris in the series it increased the severity of symptoms. Apart from 4 patients who developed acneiform dermatitis, swelling of the salivary glands, or gastrointestinal symptoms during the administration of the formic acid analogues, no side-effects were observed.

The same analogues were then given for 6 to 12 months to 7 myxoedematous patients. The basal metabolic rate was increased and a cuthyroid state could be maintained in these patients with adequate doses. The authors conclude that the p-isomers of thyroxine and triiodothyronine, apart from having some general metabolic effects, are well tolerated by patients with coronary atherosclerosis even when given in doses sufficient to produce and maintain a reduced serum cholesterol level.

Z. A. Leitner

105. Sodium dextro-Thyroxine in Coronary Disease and Hypercholesteremia

R. J. JONES and L. COHEN. Circulation [Circulation] 24, 164-170, Aug., 1961. 2 figs., 22 refs.

The authors describe the results of administration of p-thyroxine in a dosage of 4 to 8 mg. daily to 20 outpatients of the University of Chicago Clinics suffering from coronary disease or hypercholesterolaemia. In all the cases the values for the serum cholesterol level determined monthly were available for 6 months before treatment began. In 3 patients there was a sharp increase in the frequency of angina, and treatment was discontinued; one patient did not cooperate and one died suddenly while at work during the tenth week of treatment.

A marked hypocholesterolaemic effect was obtained with the drug, mainly in relation to the beta-lipoprotein fraction. The drug showed the same tendency as do other active thyroid compounds to raise basal metabolism and to aggravate angina and, occasionally, signs of congestive failure.

T. Semple

106. Anticoagulants in Acute Myocardial Infarction T. HILDEN, K. IVERSEN, F. RAASCHOU, and M. SCHWARTZ. Lancet [Lancet] 2, 327-331, Aug. 12, 1961. 1 fig., 21 refs.

An evaluation of anticoagulant therapy in acute myocardial infarction was carried out over a period of 4 years in 4 medical departments at Kommunehospitalet and Bispebjerg Hospital, Copenhagen. Each department used anticoagulants for 2 of the 4 years, so that during each year this treatment was given in 2 of the 4 departments.

The criteria of selection included electrocardiographic (ECG) signs of acute myocardial infarction either in one tracing or in sequential tracings. Altogether 800 patients were included in the trial, 371 of whom were treated with anticoagulants and 429 without. The two groups, although not equal in number, were comparable as regards sex ratio, age distribution, symptoms and signs, and ECG findings. Anticoagulant therapy was started with 25,000 units of heparin subcutaneously twice daily and continued subsequently with dicoumarol until the patient was ambulant. The prothombin level was determined by Owren's P and P method and kept within the 10 to 25% therapeutic range. Apart from anticoagulant therapy the management of the patients in the two groups was similar. Mortality was 25% in the control group and 23% in the anticoagulant group, the difference not being significant. The number of deaths from thromboembolic complications decreased as a result of therapy, but compared with the total mortality this was of little significance. Necropsy findings also demonstrated a decrease in thrombosis and embolism (pulmonary infarction, pulmonary embolism, and cardiac mural thrombi) in the patients given anticoagulants.

[This is a valuable contribution, but still does not provide a certain answer to the vexed question of the role of anticoagulant therapy in myocardial infarction. The distribution to treatment groups was not by random allocation; there were 58 more patients in the control group than in the treated group.]

A. S. Douglas

107. Observations on the Coronary Vasodilator Effect of "Persantin"

A. A. F. PEEL, K. BLUM, W. M. LANCASTER, J. L. C. DALL, and G. L. CHALMERS. Scottish Medical Journal [Scot. med. J.] 6, 403-410, Sept., 1961. 4 figs., 13 refs.

This clinical investigation into the coronary vasodilator properties of "persantin" was carried out at the Victoria Infirmary, Glasgow. Persantin is a pyrimidopyrimidine derivative which several workers, mainly in Germany, have recently reported to have a vasodilator action on the coronary vessels greatly exceeding any other effect on the circulation; these reports are briefly reviewed. In 5 patients with mitral stenosis, but without evidence of myocardial ischaemia, the coronary blood flow was measured during cardiac catheterization by estimation of the oxygen saturation of coronary sinus blood. In all 5 patients the intravenous injection of persantin in a dosage of 0.16 to 0.3 mg, per kg, body weight was followed by an increase in coronary blood flow ranging from 7 to 37% without any apparent change in the heart rate or blood pressure. The optimum dose was 0.27 mg. per kg. body weight.

The effect of a single intravenous injection of persantin on the electrocardiogram (ECG) was then studied in patients with symptoms due to ischaemic heart disease. In 6 such patients with coronary insufficiency but without recent infarction persantin in doses of up to 0.23 mg.

per kg. produced no changes in the ECG, but in 2 patients given doses of 0.27 and 0.30 mg. per kg. respectively inverted T waves became less deep or upright. Of 41 patients with recent myocardial infarction who were treated with persantin intravenously in a standard dose of 10 mg. 12-hourly for 4 days, some temporary improvement in T waves was seen in 11; in all cases, however, the T-waves became inverted again when persantin was given orally (up to 50 mg. thrice daily). In 7 patients with angina of effort single intravenous doses of 0.2 to 0.3 mg. per kg. failed to prevent the development of an ischaemic pattern in the ECG following effort. A controlled trial was also carried out on 5 patients with coronary insufficiency who were having repeated attacks of angina at rest in bed though receiving trinitrin. After an initial period of observation they were given successively intravenous persantin (10 mg, twice daily), intravenous sterile water, oral persantin (37.5 mg, twice daily), and inert tablets, these regimens being employed in a different sequence in each case. The frequency of anginal attacks was found to diminish progressively as soon as each form of treatment was begun, but this was quite independent of their order, from which it is deduced that the improvement resulted mainly from the rest in bed coupled with the knowledge that some form of treatment was being given.

[Unfortunately no over-all conclusion as to the value of persantin is offered.] -M. Harington

108. Post-myocardial-infarction Syndrome C. DAVIDSON, M. F. OLIVER, and R. F. ROBERTSON.

British Medical Journal [Brit. med. J.] 2, 535-539, Aug.

26, 1961. 2 figs., 6 refs.

A review of 500 consecutive cases of acute myocardial infarction admitted to Edinburgh Royal Infirmary revealed only 3 cases showing features of the postmyocardial-infarction syndrome, an incidence of less than 1%. Describing 5 cases of this syndrome in the present paper the authors state that the most striking clinical feature is pericardial friction. This occurs later than the pericardial friction associated with uncomplicated myocardial infarction and lasts much longer, and may be followed by evidence of pericardial effusion. Chest pain, which is usually present, differs from the original infarction pain and is dull in character, but may be aggravated by inspiration. Irregular fever and a raised erythrocyte sedimentation rate persist for weeks. In 4 of the 5 patients small pleural effusions developed. The "pneumonitis" and "periostitis" reported in other series of cases were not observed. In the authors' view the diagnosis of the post-myocardial-infarction syndrome should present little difficulty provided the physician is aware of its existence. All the patients in the present series were receiving anticoagulants, but this treatment was not considered to be a causal factor. Of 3 patients given prednisolone, 2 appeared to respond, but in one the drug had to be stopped because congestive cardiac failure developed. The ultimate prognosis appears to be good since all'5 patients recovered. It is suggested that this condition is closely related to the post-C. Bruce Perry commissurotomy syndrome:

109. Comparison of the Amount of Coronary Arteriosclerosis in Autopsied East Africans and New Yorkers R. F. Scott, A. S. Daoud, R. A. Florentin, J. N. P. DAVIES, and R. M. Coles. American Journal of Cardiology [Amer. J. Cardiol.] 8, 165-172, Aug., 1961. 8 refs.

In a combined study at Albany Medical College, New York, and Makerere College, Kampala, Uganda, the hearts of 117 East African negroes and 137 white New Yorkers were examined by the same observers for evidence of coronary arteriosclerosis. In the New York series there were 46 myocardial infarcts, 16 hearts with frésh coronary arterial thrombi and 66 with old thrombi, and 109 hearts with coronary arterial calcification, whereas in the African series no infarcts, arterial thrombi, or calcification were seen.

To provide an index of the degree of coronary arteriosclerosis the thickness of the walls of the coronary arteries was measured at fixed points by means of special callipers in 43 African and 43 American hearts from patients matched for sex and age. The thickness in the New York hearts was significantly greater, although there was some overlap between the two series. In this matched series, although the mean height of the patients in each group was almost identical, the mean weight of the New Yorkers was approximately 50% greater than: that of the Africans.

This study provides further evidence that coronary arteriosclerosis is more common and more severe in Americans than in Africans. T. B. Begg

110. The Comparative Racial Prevalence of Ischemic Heart Disease in Cape Town

V. Schrire. American Journal of Cardiology [Amer. J. Cardiol.] 8, 173-177, Aug., 1961. 22 refs.

Electrocardiograms taken at the Groote Schuur Hospital, Capetown, in 1958 and 1959 have been analysed with a view to assessing the incidence of myocardial infarction and ischaemic heart disease in the various racial groups. Electrocardiography was equally available to all patients irrespective of race, and the reporting was uniform. Altogether electrocardiograms from 9,507 patients were examined, the ratio of the 3. racial groups (white, coloured, and Bantu) being approximately 7.1:5.6:1.

Definite myocardial infarction was shown in 720 patients, 550 (76%) of whom were white, 167 (23%) coloured, and only 3 (0.4%) Bantu. A further 859 electrocardiograms showed additional abnormalities in patients with a history of angina or infarction; 596 of these patients were white, 253 coloured, and 10 Bantu. Thus the total number of patients showing electrocardiographic signs of ischaemic heart disease was 1,579, of whom 1,146 were white, 420 coloured, and 13 Bantu. Age factors did not appear to account for the difference in incidence.

Since the hospital concerned has a means test and caters only for the poorer section of the population, the richer members of the white community are excluded, so that the relative higher incidence of ischaemic heart disease in white people suggested by the electrocardiograms is probably an underestimate.

This study confirms previous findings that ischaemic heart disease is very rare in the Bantu, relatively common in those of mixed blood. T. B. Begg

111. Acute Myocardial Infarction in Ninety Negro Patients: Clinical Manifestations and Immediate Mortality. Comparison with 229 Similarly Studied White **Patients**

J. THOMAS, C. CALHOUN, C. O. T. BALL, R. S. ANDERSON, and G. R. MENEELY. American Journal of Cardiology [Amer. J. Cardiol.] 8, 178-183, Aug., 1961. 1 fig.,

Myocardial infarction has been thought to be rare in negroes, and a suggested explanation for this is that negroes tend to present with dyspnoea rather than pain. The present study was designed to examine the clinical pattern of myocardial infarction in 90 negroes admitted to George W. Hubbard Hospital, Nashville, Tennessee, over a period of 25 years; of these, 50 were male and 40 female, and at least 80 were suffering from a first attack. For comparison 229 white patients (168 male and 61 female) with myocardial infarction admitted to Vanderbilt University Hospital in the same city were also studied. Thus whereas the sex incidence in the negroes was nearly equal, the ratio of white males to females was almost 3:1. The age ranges in the two racial groups were comparable.

Angina pre-dated the infarct in 63 (79%) of the 80 negro patients in whom a previous history was obtainable, as compared with 54% in the whites; and hypertension (above 150/90 mm. Hg) was found in 43 (78%) of 55 negro patients compared with 53% in the whites. Of the total 90 negroes, 77 (85%) had pain (90% of the whites), and most of those who did not complain of pain were, for various reasons such as unconsciousness, incapable of doing so. Dyspnoea was noted in more than 50% of the negroes compared with 70% of the whites. Signs of congestive cardiac failure were present in 43 (47%) of the negroes; and 13, of whom 11 were women, were diabetic. The immediate mortality was 26% among the negroes and 41% in the white group.

It is concluded that there is no major difference in the clinical presentation of myocardial infarction in negroes as compared with white people. Hypertension is more often an associated condition in the former, and diabetes is a frequent complication in negro women. The maleto-female ratio is lower in negroes with myocardial infarction and the increased frequency of diabetes in negro women may partly account for this.

T. B. Begg

Racial Patterns of Coronary Heart Disease. Blood Pressure, Body Weight, and Serum Cholesterol in Whites and Negroes

J. STAMLER, D. M. BERKSON, H. A. LINDBERG, W. MILLER, and Y. HALL. Geriatrics [Geriatrics] 16, 382-396, Aug., 1961. 4 figs., bibliography.

An analysis of certain data concerning white and negro men employed by a utility company in Chicago and negro men and women in the low-income groups under observation by the Chicago Board of Health showed that

while the proportion of individuals with a raised blood pressure was higher in negroes than in white subjects the in white South Africans, and intermediate in incidence, incidence of atherosclerotic heart disease was not significantly higher in negroes. [This conclusion is not very well supported by the evidence cited because the disparity between the number of white persons and the number of negroes in the utility company was of the order of 10:1the total number of negroes in this group being small. Further, diastolic blood pressures of 90 mm. Hg were taken to indicate hypertension.]

A comparison of the serum cholesterol levels in both groups showed that in male negroes, particularly those in the low-income groups, the incidence of hypercholesterolaemia was lower than in white subjects. In negro women, on the other hand, the serum cholesterol pattern appeared to be more normal and the incidence of coronary heart disease did not differ markedly from the average for Chicago residents in general.

J. Robertson Sinton

HEART FAILURE

The Pulmonary Vessels in Incipient Left Ventricular Decompensation: Radiologic Obsérvations M. Simon. Circulation [Circulation] 24, 185-190, Aug., 1961. 8 figs., 16 refs.

In this paper from Beth Israel Hospital and Harvard Medical School, Boston, the author describes the characteristic radiological changes in the pulmonary vascular pattern found in left ventricular decompensation and other causes of pulmonary venous hypertension before clinical symptoms appear. In the upper zones the pulmonary veins undergo marked dilatation and the pulmonary arteries also dilate slightly. In contrast, the veins and arteries of the lower zones do not dilate and may even be narrowed. Normally, upper zone vessels are actually smaller, as in the erect posture lower lobe venous pressure is greater owing to difference in hydrostatic level. A rise in pulmonary venous pressure apparently produces a reflex constriction of veins and arteries. A critical level of venous pressure (probably about 10 to. 15 mm. Hg) first occurs in the lower lobe veins, thus causing a constriction confined to this zone. Cardiac output is maintained by diversion of blood through the upper zone vessels, producing a compensatory dilatation. A horizontal position might be expected to induce similar elevation of venous pressure and vasoconstriction in the upper zones, and this may partially explain the choice of the orthopnoeic position in these patients. An exception to this typical vascular pattern in left ventricular failure occurs in patients with severe emphysema or chronic bronchitis, where both upper and lower lobe vessels appear to become dilated.

114. Pericardial Effusion in Congestive Heart Failure W. L. WINTERS JR., B. L. CARTER, H. M. STAUFFER, and L. A. Soloff. Diseases of the Chest [Dis. Chest] 40, 82-86, July, 1961. 2 figs., 3 refs.

In this communication from Temple University Medical Center, Philadelphia, the authors advocate the use of angiocardiography using intravenous carbon dioxide in

cases of congestive heart failure in order to determine to what degree each of the two possible factors, namely, pericardial effusion and cardiac dilatation, contributes to the enlargement of the cardiac silhouette. Through the intermediary of an intravenous drip 100 ml. of CO₂ is injected rapidly into the antecubital vein and the radiograph taken in the left lateral recumbent position. The diagnosis of pericardial effusion is made if the right atrial pericardial wall is more than 4 mm. in diameter at its narrowest. In 18 patients with congestive heart failure investigated by this method gas angiocárdiography provided definite evidence of pericardial effusion in 6, of whom 4 were suffering from rheumatic heart. disease, one from hypertension, and one from coronary arterial disease. From the prognostic point of view the presence of pericardial effusion in congestive heart failure did not appear to be significant.

Although the authors claim that the method is quite safe, they admit that there is sometimes difficulty in interpreting the gas angiocardiogram on account of overlapping pulmonary structures, this often being accentuated by congestion. To overcome this difficulty they now recommend that 16-mm. cineradiography at the rate of 64 frames per second should replace the radio-P. T. O'Farrell

graphic technique.

115. Spironolactone Used with Mercaptomerin in the Treatment of Congestive Cardiac Failure

J. D. K. North, R. N. Howie, and F. H. Sims. Medical Journal of Australia [Med. J. Aust.] 2, 92-95, July 15 [received Sept.], 1961. 3 figs., 16 refs.

The value of the aldosterone antagonist spironolactone in enhancing the effect of the mercurial diuretic mercaptomerin in congestive cardiac failure was studied in 7 patients at Auckland Hospital, Auckland, New Zealand. All the patients were receiving a fixed low-sodium diet (22 mEq. per day) and a constant-potassium diet (70 . mEq. per day), with restricted fluid intake (1,600 ml. per day). Six patients had been previously treated for a month with diuretics at home with unsatisfactory results. After a 2-day control period 2 ml. of mercaptomerin was given on alternate days for 6 injections (preceded by 2 g. of ammonium chloride) and spironolactone, 800 mg. daily in divided doses, was given on days 4, 5, 8, 9, 12, and 13. The results were assessed on loss of body weight, urinary electrolyte excretion, and serum electrolyte levels.

All the patients lost weight during the trial and there was no compensatory weight gain on the days that mercaptomerin was not given; this latter phenomenon has been previously described in cases treated with mercurial diuretics and is attributed to adrenal overactivity. An increased urinary loss of sodium and chloride occurred with mercaptomerin alone in 6 patients. In only one patient did spironolactone produce a response not obtained with mercaptomerin alone. In response to mercaptomerin the urinary electrolyte excretion fell progressively with successive injections, although this tendency was somewhat offset by spironolactone. The serum electrolyte levels did not change significantly.-The authors conclude that spironolactone does not significantly augment the response to mercaptomerin in was administered in the form of tablets of 200 mg. each,

patients with congestive heart failure and should be reserved for refractory cases. It does, however, prevent the compensatory gain of weight often occurring on the day following injection of a mercurial diuretic.

Gerald Sandler

116. The Ineffectiveness of an Inotropic Agent, Mephentermine ("Wyamine"), in the Treatment of Congestive Heart Fallure

R. L. FRYE, R. L. KAHLER, and E. BRAUNWALD. American Heart Journal [Amer. Heart J.] 62, 301-303, Sept., 1961. 2 figs., 3 refs.

Mephentermine sulphate, a synthetic sympathomimetic amine, has been shown to augment strikingly the contractility of both non-failing and failing canine hearts. It acts primarily by raising the ventricular function curve and improving the efficiency of the dilated failing heart; its effect on the systemic arterial bed is minimal. The drug is apparently well absorbed from the gastrointestinal tract and toxicity is slight. In view of these properties it appeared to be an ideal drug for the treatment of chronic congestive heart failure.

At the National Heart Institute, Bethesda, Maryland, the drug was given to 6 patients, 4 of whom had chronic inactive rheumatic heart disease (3 with mitral and one with aortic incompetence), one had arteriosclerotic heart disease, and one myocardial failure of unknown actiology. All 6 patients had required a low-salt diet, digitalis, and diuretics before the trial. Mephentermine was given in a dosage ranging from 25 to 500 mg. daily; one patient received up to 200 mg. intramuscularly per day. In none of the cases did administration of the drug exert any beneficial effect on the congestive failure state. There appeared to be slight worsening of the condition in 2 patients and a transient psychosis occurred in one patient.

The authors state that these observations emphasize "that the state of clinical congestive heart failure is far more complex than the simple depression of myocardial contractility which may be induced acutely in the experimental laboratory, and which responds rapidly to sympathomimetic amines"; they would also seem to emphasize the clinical importance of treating the extracardiac manifestations of heart failure. A. J. Karlish

117. Clinical Study of a New Sulphonamide Diuretic in Cardiac Insufficiency. (Étude clinique d'un nouveau diurétique sulfamidé dans l'insuffisance cardiaque) P. Soulié, B. Morin, R. Pariente, F. Cerf, and A. BENASERRAF. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 37, 2553-2564, Sept. 14, 1961.

This paper from the Hôpital Broussais, Paris, reports a clinical trial of a new sulphonamide diuretic, "aquedux" (4-chlorobenzol-1:3-disulphonamide), in patients with cardiac oedema. Previous experiments on laboratory animals showed that this drug has considerable diuretic activity, both aqueous and electrolytic, and very slight toxicity. The mode of action is so far unknown. Of the 25 patients with heart failure in the trial, 18 had "global" failure, 2 cor pulmonale, 3 constrictive pericarditis, and 2 purely left ventricular failure. The drug

and each patient received 3 tablets a day for 3 days a week during 2 consecutive weeks. The treatment was associated with a low-sodium diet and cardiotonics as required.

Aquedux in oral tablet form was found to have considerable diuretic activity almost equal to that of intravenous mercurial diuretics. In no case were serious complications, either hepatic or renal, observed, and no blood dyscrasia was produced; moderate hypokalaemia, which did not necessitate interruption of treatment, occurred in 3 cases and was successfully treated with supplements of potassium chloride. The new drug was equally effective in maintenance treatment of heart failure, particularly that associated with oedema. The effect on the arterial blood pressure was slight; however, the drug has not been used in hypertensive patients, but purely as a diurètic in cardiac oedema. A. J. Karlish

HYPERTENSION .

118. Essential Hypertension and Inheritance of Vascular Reactivity

A. E. Doyle and J. R. E. Fraser. Lancet [Lancet] 2, 509-511, Sept. 2, 1961. 1 fig., 8 refs.

The response to intra-arterial injections of nóradrenaline in the sons (25) of parents with normal blood pressure was compared with that in a group of young men (26) whose parents were known to have high blood pressure and were attending the hypertensive clinics at the Royal Melbourne Hospital, Victoria, and the Alfred Hospital, Melbourne. The reduction in blood flow in the sons of hypertensive patients was significantly higher than that in the sons of normotensive subjects. The results of this investigation add support to the view that hypertension is, in part, genetic in origin, at least so far as the response to abnormal stress or stimulation is concerned.

J. Robertson-Sinton

119. Serum Sodium and Potassium in Essential Hypertension

B. E. LEVINE, J. M. WELLER, and R. D. REMINGTON. Circulation [Circulation] 24, 29-33, July, 1961. 16 refs.

In this paper from the University of Michigan Medical School, Ann Arbor, a study is reported of the serum electrolytes in 50 healthy normotensive patients and in 43 patients with uncomplicated essential hypertension, data concerning the serum sodium and serum potassium levels and the "stated dietary salt intake" being subjected to statistical analysis. No significant difference was observed between the two groups in respect of the mean serum sodium and potassium levels. Further, no association was found between the stated salt intake and the mean blood pressure, a past history of raised blood pressure, the serum sodium level, or the serum potassium level.

The authors state that the findings of other workers, which they discuss, are not consistent. Their own observation (and also of some other workers) that there is no relationship between a raised blood pressure and salt intake contrasts with experimental evidence that high-sodium diets may produce hypertension and that

this may be prevented by a high potassium intake. "If a relationship exists between salt intake and hypertension it is a highly complex one."

J. S. Malpas

120. Individual Renal Clearance in Diagnosis of Hypertension of Renal Origin

D. F. McDonald. Journal of Urology [J. Urol. (Baltimore)] 86, 289-293, Sept., 1961:

Studies are reported from the University of Rochester School of Medicine, New York, of 107 patients who showed features suggestive of unilateral renal hypertension and who were examined by bilateral ureteral catheterization performed during the constant intravenous infusion of inulin and para-aminohippurate (PAH). Samples of blood and urine were analysed for their content of inulin, PAH, sodium, potassium, ammonium, chloride, and urea, and for osmolarity. The procedure failed in 10 cases—because of leakage of urine into the bladder in 5, unsuccessful ureteral catheterization in 2; and inadequate secretion of urine from one kidney for chemical analysis in 3. Of the remaining 97 patients, features suggestive of unilateral renal hypertension amenable to surgery were considered to be present in 42, and of these, 29 accepted this recommendation. As the result of operation 13 of the 21 patients who underwent nephrectomy, one of the 2 who underwent partial nephrectomy, and one out of 6 subjected to renal arterial surgery obtained sustained remission of the hypertension. The causes of failure in the 8 patients who were not benefited by nephrectomy are discussed.

Retrospective analysis of "split function" studies showed that pyelography and renography with ¹³¹I"hippuran" had little prognostic value; likewise disparity in urinary volume from the two kidneys, excretion studies with phenolsulphonphthalein, and determination of urinary sodium and ammonia concentrations were seldom helpful. On the other hand studies of reduced inulin, PAH, and osmolar clearances were most helpful in suggesting unilateral renal ischaemia as a curable cause of hypertension.

K. G. Lowe

121. Treatment of Hypertension with Benzydroflumethiazide as the Sole Antihypertensive Agent

R. W. P. Achor, K. G. Berge, R. W. Gifford Jr., and H. L. Mason. New England Journal of Medicine [New Engl. J. Med.] 265, 457-462, Sept. 7, 1961. 21 refs.

Writing from the Mayo Clinic, the authors describe a trial of benzydroflumethiazide in hypertensive patients. This drug is a fluorine-containing derivative of the benzothiadiazine group of compounds which are active as diuretics. The series consisted of 21 patients (17 of them women) with blood pressures over 165/95 mm. Hg who had not received any specific antihypertensive medication and none of whom had papilloedema or retinal haemorrhages or exudates. The study was carried out as a double-blind trial over 4 months, the active drug (D) in a dosage of 5 mg, twice daily and a placebo (P) being administered for one or 2 months at a time in the following sequences: PPDD, DDPP, PDDP, or DPPD.

During the periods of treatment with benzydroflumethiazide the blood pressure fell by an average of 19 mm. Hg systolic and 7 mm. diastolic more than during the periods of placebo administration, a difference which was found to be significant at the 2% level. In 5 of the patients there was no reduction in blood pressure. A slight increase in pulse rate and a small decrease in body weight were noted during treatment with the active drug. Side-effects were transient and infrequent. Biochemical changes noted in the blood during treatment with the drug included substantial falls in the plasma potassium and chloride levels, a rise in the plasma bicarbonate and uric acid levels, and a small increase in the blood urea level.

The authors conclude that benzydroflumethiazide is a useful addition to the benzothiadiazine group of drugs, particularly because of its greater potency (on a weightfor-weight basis), but that in antihypertensive activity and in its tendency to produce potassium depletion the new drug does not differ significantly from the other known thiazide diuretics.

M. Harington

122. Guanethidine and Hydrochlorothiazide in the Treatment of Hypertension

G. Blanshard and W. Essigman. Lancet [Lancet] 2, 334-336, Aug. 12, 1961. 12 refs.

A comparative trial of guanethidine alone and combined with hydrochlorothiazide in the treatment of hypertension was carried out at the Central Middlesex Hospital, London. Of 65 patients with severe hypertension (8 in the malignant phase), satisfactory control of blood pressure was obtained in 57 (with guanethidine alone in 45, with guanethidine and chlorothiazide in 12). In 8 patients (5 in the malignant phase) the response was unsatisfactory because of severe diarrhoea (2 patients), nocturnal breathlessness (2), inability to ejaculate (one patient), increase in stress incontinence (1), slow response to treatment requiring change to pempidine (1), and cerebral haemorrhage shortly after starting treatment (1).

A group of 22 patients in whom blood pressure was satisfactorily controlled with guanethidine were given tablets containing 10 mg. of guanethidine, 10 mg. of hydrochlorothiazide, and 600 mg. of potassium chloride. In 20 of the patients the dose of guanethidine necessary in the combined tablet was less than that of guanethidine when given alone. In 6 patients in this group there was some reduction in side-effects, but in 7 others side-effects developed for the first time when the combination of drugs was given.

K. G. Lowe.

123. Guanethidine in the Ambulatory Treatment of Arterial Hypertension. [In English]

A. GALSKOV, E. CLAUSEN, T. HILDEN, and A. R. KROGS-GAARD. Acta medica Scandinavica [Acta med. scand.] 170, 31-42, July, 1961. 19 refs.

Guanethidine lowers the blood pressure through blockade of the sympathetic nervous system, but has no effect on parasympathetic function, in contrast to the mode of action of ganglion-blocking drugs. In this trial, carried out at Bispebjerg Hospital, Copenhagen, on 42 patients suffering from essential hypertension and followed up for 12 months as out-patients guanethidine caused a marked fall in blood pressure in 23 patients and

a satisfactory fall in another 7, but in the remaining 12 cases treatment had to be discontinued because of sideeffects. The action of the drug was found to be gradual and prolonged, so that it was possible to treat patients with one single daily dose and still obtain a uniform effect on blood pressure. As in the case of ganglion-blocking agents, the tendency to orthostatic hypotension limited the usefulness of the drug. Among other side-effects. diarrhoea and weakness were the most common, but they did not necessitate stopping treatment, whereas fluid retention was the most serious drawback and the main reason for withdrawal of the drug. The authors advocate the simultaneous administration of a diuretic to prevent such fluid retention, which may lead to oedema and pulmonary venous congestion; moreover, the diuretic also enhances the hypotensive action of guanethidine and permits a reduction in the dosage of this drug.

A. I. Suchett-Kaye,

124. Drug Therapy of Hypertension. V. Observations on the Results with Ganglion-blocking Agents Given in Combination with Rauwolfia and Chlorothiazide

J. H. Moyer and A. N. Brest. Archives of Internal Medicine [Arch. intern. Med.] 108, 231-247, Aug., 1961. 12 figs., bibliography.

This is a careful assessment of the effect of rauwolfia and ganglion-blocking drugs on hypertension. The most effective combination was found to be that of rauwolfia, mecamylamine, and chlorothiazide. Guanethidine was not included in the trial. Special mentions made of the need to watch renal function if the blood pressure is profoundly lowered and of the fact that the side-effects of the ganglion-blocking drugs are mainly those of parasympathetic blockade. G. S. Crockett

BLOOD VESSELS

125. Aortic Arch Syndrome with Special Reference to Rheumatoid Arteritis. [In English]

H. SANDRING and G. WELIN. Acta medica Scandinavica [Acta med. scand.] 170, 1-19, July, 1961. 4 figs., 41 refs.

This paper reviews the aortic arch syndrome, with special reference to aetiology, and is based on data collected from 24 cases investigated in the Department of Medicine, Mölndal, Sweden. The patients could be divided into three groups according to the actiology: (1) 15 patients, all female, with the Takayashu syndrome, most of whom had a history of rheumatic disease or a disorder of the lupus-erythematosus type; (2) 3 patients with considerable scarring of the neck in whom the actiology was considered to be extravasal; (3) 6 patients suffering from atherosclerosis which was causing the syndrome. The most constant clinical findings were systolic murmurs in the neck region, pulsation indicating collateral circulation in the affected area, and a difference in amplitude of the right and left radial pulses. Radiological examination, including angiography of the affected vessels, was necessary for a correct diagnosis. It is stated that in 75% of cases of this syndrome rheumatic disease can be regarded as causative, in spite of the fact

that no clear evidence of rheumatic disease has been found in all cases. The advent of steroid treatment has improved the prognosis for patients suffering from Takayashu arteritis.

A. I. Suchett-Kaye

126. Embolization from the Atria in Arteriosclerotic Heart Disease

D. T. Beer and B. GHITMAN. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 287-291, Aug. 5, 1961.

Out of 1,000 cases which came to necropsy at the Montefiore Hospital. New York, the authors selected for examination those with rheumatic or arteriosclerotic heart disease to determine the relative frequency of peripheral embolism from the atria in the presence or absence of fibrillation. There were 295 cases of arteriosclerotic heart disease, and in 52 of these auricular fibrillation was recorded during life. Only one case of embolism arising from the atrium (2%) was found among these 52 cases, and 2 cases (1%) occurred among the remainder. Among 91 cases of rheumatic heart disease the authors found a 38% incidence of embolism in the presence of fibrillation and an incidence of 25% when it was absent. They consider that in many of these cases the embolus arose from the right atrium, though the various other possible sources of embolism are also discussed. They make the point that in the absence of rheumatic heart disease the chances of embolism arising from the left atrium, even when fibrillation is present, are statistically insignificant. J. B. Wilson

PULMONARY CIRCULATION

127. A Study of Pulmonary Embolism. Part I. A Clinicopathological Investigation of 100 Cases of Massive Embolism of the Pulmonary Artery; Diagnosis by Physical Signs and Differentiation from Acute Myocardial Infarction

L. W. GORHAM. Archives of Internal Medicine [Arch. intern. Med.] 108, 8-22, July, 1961. 39 refs.

A review of the literature suggests that the diagnostic error in pulmonary embolism in 50%. This is partly because there are many symptoms and signs common to both pulmonary embolism and acute myocardial infarction—for example, anterior chest pain, pallor, cyanosis, dyspnoea, tachycardia, arrhythmia, feeble heart sounds, hypotension, sweating, fever, and leucocytosis. Errors may also be due to inadequate clinico-pathological studies and teaching.

In the present paper the author discusses the diagnosis of pulmonary embolism by physical signs and its differentiation from myocardial infarction on the basis of the clinical records of 100 cases of massive pulmonary embolism found among 5,700 necropsies conducted at the New York Hospital-Cornell Medical Center. A classification of types of case based on necropsy findings is given. A list of 12 physical signs, one or more of which may result from obstruction of the pulmonary artery or its main branches, is then presented and these are discussed. They are: (1) pulsation in second left

interspace; (2) accented P₂ greater than A₂; (3) pseudoor pleuro-pericardial friction; (4) systolic murmur in • second left interspace; (5) diastolic murmur in second left interspace; (6) interscapular bruit; (7) unilateral expansion lag with diminished breath sounds; (8) increased cardiac dullness to the right; (9) increased jugular venous pressure, aggravated by compression of the liver; (10) gallop rhythm in second and third left interspaces; (11) enlarged liver; and (12) die rote Blutwelle (a red wave passing quickly over the pallid cyanotic face when obstruction is temporarily relieved).

D. Goldman

128. A Study of Pulmonary Embolism. Part II. The Mechanism of Death; Based on a Clinicopathological Investigation of 100 Cases of Massive and 285 Cases of Minor Embolism of the Pulmonary Artery

L. W. GORHAM. Archives of Internal Medicine [Arch. intern. Med.] 108, 189-207, Aug., 1961. 1 fig., 39 refs.

After an extensive review of the literature on the mechanism of death in cases of pulmonary embolism the author describes the necropsy findings in 385 cases seen at the New York Hospital-Cornell Medical Center. In 285 of the cases there were only small emboli in the lesser branches of the pulmonary artery, while the main stem and both major branches were free. In the author's view the infarction in 199 of the 285 cases was incidental and not related to the cause of death, while in 49 there was already advanced right ventricular failure and further infarction mechanically aggravated this condition. Death in the remaining 37 cases might heretofore have been attributed to a reflex mechanism—for example, release of serotonin-but further analysis indicated that only 14 deaths (5% of the series) were reflex and not the result of underlying disease.

A number of illustrative cases are described and the results of animal experiments reviewed. The author finally discusses the case for and against the theory that sudden death following minor pulmonary embolism is due to reflex causes.

D. Goldman

129. A Study of Pulmonary Embolism. Part III. The Mechanism of Pain: Based on a Clinicopathological Investigation of 100 Cases of Minor and 100 Cases of Massive Embolism of the Pulmonary Artery

L. W. GORHAM. Archives of Internal Medicine [Arch. intern. Med.] 108, 418-426, Sept., 1961. 33 refs.

Of 100 cases of pulmonary infarction seen at necropsy at New York Hospital—Cornell Medical Center, pleural pain had occurred in 22. Study of the literature showed that the pain is due to tension on the sensory nerve endings in the parietal pleura and does not result from the rubbing together of two inflamed pleural surfaces. Of 100 patients who died from massive pulmonary embolism, 19 had a history of precordial or substernal pain indistinguishable from that of acute myocardial infarction. In 4 of the 19 the pain had radiated to the left arm.

The mechanisms of this angina-like pain are discussed at length. The author considers that it is due to acute pulmonary hypertension with stimulation of the sensory nerve endings in the vessel walls.

D. Goldman

Clinical Haematology

130. Androgens and Erythropolesis, I. Preliminary Clinical Observations

F. H. GARDNER and J. C. PRINGLE JR. Archives of Internal Medicine [Arch. intern. Med.] 107, 846-862, June, 1961. 11 figs., bibliography.

The fact that the erythrocyte count, total erythrocyte volume, and haemoglobin and haematocrit values are higher in men than in women suggests that erythropoiesis and the elaboration of sex hormones are intimately related. This paper from Harvard Medical School, Boston, reports the results of a trial, begun in 1956, of the effects of androgenic hormones in the treatment of refractory anaemia occurring in 54 patients with a variety of diseases, including myelomatosis, myeloid metaplasia, Hodgkin's disease, and leukaemia. All had previously received the accepted treatment for their primary disease, without amelioration of the anaemia. Of the hormones used, methýltestosterone and fluoxymesterone were given by mouth and testosterone enanthate, testosterone propionate, and testosterone cyclopentylpropionate intramuscularly in oil. Treatment was continued for various periods up to 16 months and the doses used were pharmacological rather than physiological. Results were assessed by conventional haematological observations on the peripheral blood and in some cases by the use of erythrocytes labelled with radioactive iron or radioactive chromium.

The tabulated results show that more than half the patients appear to have benefited. Improvement of the anaemia was not rapid and was not usually observed until after 4 to 6 weeks of treatment. The response, it is thought, is due to a specific increase in erythropoietic activity, although some patients with myeloid metaplasia also showed an increase in blood platelet levels. However, in the presence of increased haemolysis, whether in paroxysmal nocturnal haemoglobinuria or in association with erythrocyte-adsorbed antibody, androgens appeared to be without effect in protecting the erythrocytes from early destruction. Although all the usual complications of androgen therapy were observed, the only serious toxic effect was the occurrence of jaundice in 5 patients given methyltestosterone. A. G. Baikie

- 131. Circulatory Studies in Slowly Developing Anaemias. [Monograph, in English]
- H. BACKMAN. Scandinavian Journal of Clinical and Laboratory Investigation [Scand. J. clin. Lab. Invest.] 13, 1-94, Suppl. 57, 1961. 14 figs., bibliography.
- 132. Reproducibility and Reliability of the Schilling Test J. F. Adams and D. A. Seaton. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 67-75, July, 1961. 3 figs., 5 refs.

The Schilling test, in which the urinary excretion of radioactive vitamin B₁₂ (cyanocobalamin) is measured as an index of the absorption of the vitamin, was carried

out 6 times on each of 7 patients with pernicious anaemia studied at the Western Infirmary, Glasgow, and the Royal Infirmary, Edinburgh. The values for urinary radioactivity were all below 7.5% which is the usual accepted : upper limit in pernicious anaemia. The test was then repeated, again 6 times, after each patient had received in addition a single dose of 15 mg, of intrinsic factor. The mean values were now all greater than 7.5% and significantly greater than those obtained in the tests without intrinsic factor. In 4 patients, however, some of the individual tests gave values lower than 7.5%; in 2 of these the mean value for the 6 tests was raised, but not significantly so, by doubling the dose of intrinsic factor, while quadrupling the dose raised the value still farther in both cases, although to a significant level in only one, and now no values below 7.5% were obtained. Similar studies on 2 patients who had undergone total gastrectomy indicated an absorption defect comparable with that in pernicious anaemia, but in these patients the degree of correction by a single dose of intrinsic factor was significantly less. In one patient with coeliac disease given 6. Schilling tests values of less than 7.5% were obtained in 3 tests and greater than 7.5% in 3, the mean value for all 6 being 5.2%. This mean value was not significantly raised by the administration of calcium gluconate.

It is concluded that these findings show the reliability of the Schilling test in demonstrating impaired absorption of vitamin B₁₂ in pernicious anaemia and after total gastrectomy, but a single test in coeliac disease may be uninformative. The effect of intrinsic factor, however, is variable, and single tests may give misleading results, unless the dose is adequate; the determination of what is an adequate dose, however, is difficult and repeated testing may be necessary to establish a diagnosis of deficiency of intrinsic factor. The varied response to intrinsic factor in this study suggests that the absorption defect following total gastrectomy differs from that in pernicious anaemia.

J. L. Markson

133. Intrinsic Factor: Active and Inhibitory Components from the Mitochondria of Human Gastric Mucosal Cells

W. H. TAYLOR, B. J. MALLETT, and K. B. TAYLOR. *Biochemical Journal* [*Biochem. J.*] 80, 342–348, 1961. 3 figs., 18 refs.

Material with intrinsic-factor activity extracted from human gastric mucosa was found to occur in two forms, one attached to the mitochondria and the other dissolved in the particle-free supernatant obtained after repeated ultracentrifuging. Material with intrinsic-factor activity prepared from the mitochondria (Substance E) appeared to behave on electrophoresis and ultracentrifuging as a single molecular aggregate. However, it was shown to split into two components at pH 5 or lower. One of these components had intrinsic-factor activity, but the

other caused inhibition of this activity. It is concluded that a part of the intrinsic-factor activity of gastric mucosal cells is located on the mitochondria in association with a substance which inhibits its activity.

H. Harris

134. Intravenous Iron-Dextrin in Iron-deficiency

J. FIELDING. British Medical Journal [Brit. med. J.] 2, 279-283, July 29, 1961. 4 figs., 37 refs.

Iron-dextrin contains 20 mg. Fe per ml. in isotonic solution and is stable in saline and plasma; it has a pH of 7.3. This preparation has been used (as "astrafer") at the Paddington General Hospital, London, in the treatment of established iron-deficiency anaemias. Because the reactions obtained with previous parenteral iron preparations are in part due to haemolysis, the haemolysis caused by these products was studied. It was found that saccharated iron oxide caused more haemolysis than iron-dextran, which also caused more haemolysis at higher concentrations than iron-dextrin. The rate of plasma clearance of iron-dextrin and irondextran was also compared. It was found that after each injection of iron-dextrin the serum iron level fell to its original level, whereas in the case of iron-dextran there was a gradual increase in the serum iron level.

The results of intravenous treatment with iron-dextrin in 2 groups of patients are described. Group 1 consisted of 25 patients with iron-deficiency anaemia and a haemoglobin level of 68% or less. Haematological improvement was obtained in 24 cases, only one case (of bronchial carcinoma) failing to respond. The mean haemoglobin value before treatment was 51.2%, whereas after treatment it was 81.6%. The utilization of the injected iron showed that there was a 1% increase in haemoglobin level for every 36 mg. of iron injected. In Group 2 were 45 women with anaemia of pregnancy whose haemoglobin levels were below 70%; 26 of these were analysed after an adequate period of observation. The mean haemoglobin value before treatment was 59.3% and after treatment 80.9%. In this group a 1% rise in haemoglobin level was produced by 41 mg. of iron. The injections gave rise in a few cases to a minor inflammatory reaction around the vein; no thrombophlebitis or pain along the course of the vein was observed. There were 2 mild general reactions in Group-1 patients, but none in Group 2.

The iron-dextrin complex appeared to be as well utilized as both iron-dextran and saccharated iron oxide preparations used by other workers. Local reactions to iron-dextrin were less frequent than is usual with other intravenous preparations, and there were fewer general reactions than have been reported with iron-dextran. The author suggests that this is because of the low haemolytic action of iron-dextrin, suggesting little ionic release, and its rapid plasma clearance, which is maintained after successive injections. The advantages of intramuscular or intravenous iron therapy are discussed. The disadvantage of the intramuscular route that a proportion of the injected dose is retained in the muscle, together with its possible carcinogenic action, is considered to be sufficient to counterbalance the

obvious practical advantages of this method of administration. Iron-dextrin has probably the same order of carcinogenicity as iron-dextran and should not be used by the intramuscular route. The author suggests that the intravenous route has the merit of encouraging careful attention to the indications for parenteral iron.

R. F. Jennison

135. Autoimmune Haemolytic Anaemia: Three Cases with Antibodies Specifically Active against Stored Red Cells

W. J. JENKINS and W. L. MARSH. Lancet [Lancet] 2, 16-18, July 1, 1961. 4 refs.

This paper from the North-East Metropolitan-Regional Blood Transfusion Centre, Brentwood, Essex. reports three examples of antibodies-which reacted specifically with antigens developing in the erythrocytes of stored blood. No reaction occurred with fresh cells. from the same donors and it is suggested that the antibodies may be present in an inactive form and arise during storage by the action of intracellular enzymes reacting with a basic substrate normally present in all erythrocytes. The antigen is quite distinct from any known blood group system and from the antigens which react with cold autoantibodies. In this case the antibodies occurred in the serum of 3 women with autoimmune haemolytic anaemia; in all 3 positive Wassermann and Price precipitation reactions were obtained, these being presumably false positive results associated with the anaemia, since in one case studied in detail the Treponema pallidum immobilization (T.P.I.) test was negative. Although these 3 cases were encountered within the space of 2 years, they were the only ones met with in the examination of many thousands of sera, so that the condition must be very rare. The serological reactions in one case are described in detail.

R. B. Thompson

136. Decreased Erythrocyte Survival in Hemoglobin H Disease as a Result of the Abnormal Properties of Hemoglobin H: the Benefit of Splenectomy

D. A. RIGAS and R. D. KOLER. *Blood* [Blood] 18, 1-17, July, 1961. 7 figs., 29 refs.

Haemoglobin H gives rise to stained inclusions of denatured haemoglobin when erythrocytes containing it are incubated with brilliant cresyl blue as for a reticulocyte preparation. Relatively few individuals with this abnormal haemoglobin have as yet been recognized and the genetical basis for its occurrence is still uncertain. It seems likely that haemoglobin H occurs in individuals who are doubly heterozygous for a gene for haemoglobin H and a gene for thalassaemia (hereditary leptocytosis).

This paper from the University of Oregon Medical School, Portland, reports the study of a brother and sister who had haemoglobin-H disease and haemolytic anaemia and who were studied before and after splenectomy. By the usual clinical and haematological criteria both patients benefited from the operation, but both remained anaemic, and liable to haemolytic crises. Before splenectomy the erythrocytes of both patients had a finite life span of 40 to 45 days, with an additional random destruction of cells. After operation the finite life span returned to

normal in both cases, but random destruction was only slightly reduced. The erythrocyte survival time in the daughter of the female patient, who had thalassaemia but no haemoglobin H, was found to be normal. It is suggested that it seems likely that in erythrocytes aged 40 to 45 days haemoglobin H, when present, is irreversibly precipitated to form inclusion bodies and that the presence of these inclusion bodies leads to the rapid destruction in the spleen of the cells which carry them. After splenectomy such cells are not destroyed and their content of unaltered haemoglobin A continues to partici-,pate in oxygen and carbon dioxide transport. The random destruction of crythrocytes carrying haemoglobin H is due to the irreversible precipitation of that haemoglobin when deoxygenated and is unrelated to the age of the erythrocyte. This random destruction occurs mainly in the capillary bed and is largely unaffected by splenec-A. G. Baikie ·

137. Pyrimethamine in the Treatment of Polycythaemia Rubra Vera

D. E. Pegg and H. T. Ford. British Medical Journal [Brit. med. J.] 2, 617-621, Sept. 2, 1961. 6 figs., 14 refs.

Conflicting reports on the value of pyrimethamine in the treatment of polycythaemia rubra vera have appeared in the literature. The authors of this paper from Westminster Hospital, London, describe 5 consecutive cases in relapse which were successfully treated with pyrimethamine for periods of 7 months to 2 years; in 4 of the cases treatment had previously been given with radioactive phosphorus. In all 5 cases pyrimethamine caused a steady fall in the haemoglobin level, the packed cell volume, and the erythrocyte count in the peripheral blood after an initial time lag of 2 to 3 weeks, the patients becoming symptom-free within 5 to 8 weeks. The effect was due to a marked reduction in the erythrocyte output.

The initial dosage of the drug by mouth varied considerably—from 25 to 200 mg. daily—because of the wide variation in individual response. It was found that by using the rapidly responding reticulocyte count the correct dosage could be selected for each patient quite quickly. Side-effects in this series were minimal; epigastric discomfort occurred in 2 cases and epistaxis in one when a dosage of 50 mg. or more was given. At the correct therapeutic dosage side-effects were absent. Megakaryocyte activity and myelopoiesis were depressed at high dosage, but the platelet and leucocyte counts were not affected by maintenance doses of pyrimethamine.

The authors conclude that pyrimethamine by mouth provides an effective treatment for polycythaemia rubra vera, but its potential toxicity necessitates meticulous haematological control, particularly at the beginning of treatment.

A. Ackroyd

138. Seasonal Incidence of Clinical Onset of Hodgkin's Disease

M. D. CRIDLAND. British Medical Journal [Brit. med. J.] 2, 621-623, Sept. 2, 1961.

In the course of a review of 269 histologically proven cases of Hodgkin's disease seen at the Royal Marsden Hospital, London, since 1945, the author observed a

high incidence of clinical onset in the month of December. By selecting only those cases in which: (1) the month of onset in England was definitely known, (2) lymphadenopathy was localized to one peripheral site at onset, (3) no evidence of generalized disease was present, and (4) there was no evidence of deeper involvement within 6 months of onset a total of 106 cases were regarded as suitable for analysis of a possible seasonal association.

There was clinical onset of Hodgkin's disease in the month of December in 23 (21.7%) of the cases, the next highest incidence occurring in January with 14 (13.2%) of the cases. The same seasonal incidence was observed when the patients were divided into two groups according to the period in which the disease started (1945-54 and 1955-9). Further, the seasonal incidence was essentially the same for both sexes. The occurrence of any upper respiratory tract infection at the time of onset in 11 patients did not lead to the discovery of lymphadenopathy, nor was the relative incidence of sore throat greater in the month of December. The author states that "although the inception of recurrence is impossible to establish", peripheral node recurrence in 89 cases showed no striking seasonal incidence, nor was any particular seasonal incidence of onset found in a series of 48 cases of lymphosarcoma and reticulosarcoma. The results might support the view that Hodgkin's disease is caused by an infective agent or its onset precipitated by such an agent. A. Ackroyd

139. Irradiation and Marrow Infusion in Leukemia: Observations in Five Patients with Acute Leukemia Treated by Whole-body Exposures of 1,400 to 2,000 Roentgens and Infusions of Marrow

E. D. THOMAS, E. C. HERMAN JR., W. B. GREENOUGH III, E. B. HAGER, J. H. CANNON, O. D. SAHLER, and J. W. FERREBEE. Archives of Internal Medicine [Arch. intern. Med.] 107, 829-845, June, 1961. 6 figs., 23 refs.

At the Mary Imogene Bassett Hospital, Cooperstown, New York, 5 patients with acute leukaemia were treated by whole-body irradiation followed by infusion of bone marrow.

The doses of radiation varied from 1,400 to 2,000 r. given at rates of up to 2r. per minute; the marrow donors were in one case a parent, in 2 cases sibs, and in 2 cases an identical twin. Three of the 5 patients died from infection within 22 days, and in only one of them was there evidence of successful marrow grafting. In the 4th patient death occurred after 20 days; this patient had jaundice of unknown actiology, but at necropsy there was evidence of some marrow recovery. In the 5th case marrow function returned, but the patient died from recurrent leukaemia after 72 days. It was considered particularly disappointing that in this case whole-body irradiation with 2,000 r. was apparently inadequate to extirpate the leukaemic cells. The possibility is discussed that existing leukaemic cells were in fact destroyed, but that reactivation occurred because of the persistence of a causative sub-cellular agent.

A. G. Baikie

Urogenital System

140: An Evaluation of Maximal Water Diuresis in Chronic Renal Disease. I. Normal Solute Intake C. R. KLEEMAN, D. A. ADAMS, and M. H. MAXWELL. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 169–184, Aug., 1961. 7 figs., 27 refs.

In this study, reported from the University of California, Los Angeles, the maximum urine diluting capacity was investigated in 27 patients (selected as being in a stable state of azotaemia) suffering from various forms of chronic renal disease. After drinking a litre of water the patients were given over a 5-hour period a continuous. intravenous infusion of 2.5% dextrose solution at a rate equal to the concomitant urine flow. Comparison of the parameters of maximum water diuresis was made between the patients and healthy subjects or patients with normal renal function at equivalent rates of solute excretion per unit of functioning mass (the glomerular filtration rate being used as a reasonable approximation of functioning mass). It was shown that urinary flow and free water clearance were decreased and minimum urinary osmolarity was increased in the patients with chronic renal disease as compared with the control group. However, when these parameters of maximum water diuresis were plotted against the predicted rate of solute excretion for normal renal mass the results were quantitatively comparable in the two groups. In contrast, the maximum urinary concentration was consistently less than that predicted from relative osmotic diuresis per nephron in the patients with chronic renal disease; none of these 27 patients had fixed osmolarity (isosthenuria). Two patients could not concentrate the urine to an osmolarity equivalent to that of plasma and were classified as "mild acquired nephrogenic diabetes insipidus ".

(Since completion of this study the authors have encountered a case of "salt-losing nephritis" with a true defect in urinary dilution manifested by the fact that the patient was unable to dilute his urine below the osmolarity of the plasma.) - K. G. Lowe

141. An Evaluation of Maximal Water Diuresis in Chronic Renal Disease. II. Effect of Variations in Sodium Intake and Excretion

D. A. ADAMS, C. R. KLEEMAN, L. H. BERNSTEIN, and M. H. MAXWELL. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.*] 58, 185–196, Aug., 1961. 6 figs., 17 refs.

In their preceding study [see Abstract 140] the authors showed that the apparent defect in urinary dilution in chronic renal disease could be explained by an increased solute load within the residual nephrons, but that there is a true defect in urinary concentration. In order to test whether a reduction in solute load would improve the maximum diluting capacity without appreciably correcting the concentrating defect sixteen studies were

carried out on 15 patients with stable chronic renal disease and azotaemia during two dietary periods, in one of which a high daily intake of sodium chloride (90 to 175 mEq.) was given and in the other a low daily intake (10 mEq.).

These studies showed that dietary restriction of sodium significantly lowered the minimum urinary osmolarity during a sustained water diuresis in 14 out of 16 studies, while free water clearance increased in 11 and 11 the rate of solute excretion fell in 14 of the studies. Although the free water clearance per 100 ml. of normal renal mass (corrected on the basis of normal glomerular filtration rate) increased as solute excretion (similarly corrected) decreased during sodium restriction in 12 of the study periods, the magnitudes of these two changes did not show close correlation. Sodium restriction produced no consistent change in maximum urinary concentration or in the osmotic urine:plasma ratio. It is concluded that these findings support the contention that diluting capacity is normal in the residual nephrons, in chronic renal disease, in which, however, there is a true defect in concentrating capacity. K. G. Lowe

142. Distal Tubular Function in Chronic Hydronephrosis G. M. Berlyne. Quarterly Journal of Medicine [Quart. J. Med.] 30, 339-355, Oct., 1961. 6 figs., 28 refs.

The ability of the kidneys to acidify and to concentrate the urine was assessed in 7 patients at Manchester Royal Infirmary with established hydronephrosis. Of the 7 patients 6, who were given a standard load of ammonium chloride, were unable to attain normal degrees of urinary acidity, and the amount of ammonia produced was also low in absolute terms, though not in relation to urinary pH. Ability to concentrate the urine was also impaired in varying degree, the obligatory loss of water being notable in 3 patients. After relief of the obstruction, when this was possible, acidification and concentration improved. The part played by the loss of nephrons is discussed, but it was found that some of the findings could not be fully accounted for on this basis.

D. A. K. Black

143. Urinary Excretion of Iron-binding Protein in the Nephrotic Syndrome

D. RIFKIND, H. M. KRAVETZ, V. KNIGHT, and A. L. SCHADE. New England Journal of Medicine [New Engl. J. Med.] 265, 115-118, July 20, 1961. 2 figs., 7 refs:

This paper from the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, reports a study of the urinary excretion and serum level of siderophilin (transferrin) in 2 cases of the nephrotic syndrome. In the first patient, a 20-year-old woman with systemic lupus erythematosus in whom a renal biopsy revealed a membranous glomerulonephritis, the daily urinary excretion of total protein ranged from 13-9 to 19 g., and those

of siderophilin and iron were 1,302 mg. and 534 μ g. respectively. Although there was an increase in iron excretion to 1,000 μ g. per day following a course of intramuscular dextran-iron supplying 1,250 mg. of elemental iron in 14 days, the loss of siderophilin in the urine was virtually unchanged. During a steroid-induced remission the daily total protein excretion fell to 3 3 g. and that of siderophilin to 137 mg., while there was a reciprocal rise in the iron-binding capacity of the serum from approximately 100 to 219 μ g. of iron per 100 ml., the serum iron level and haemoglobin value remaining constant.

The second patient, a man aged 27 admitted with "idiopathic nephrosis", was shown by renal biopsy to have chronic pyelonephritis. In this patient the urinary excretion of total protein was 14.8 g. per day and of siderophilin 656 mg, per day. The urine contained 120 μ g. of iron per day, the serum iron level was 12 μ g. per 100 ml., and the total iron-binding capacity of the serum was 180 μg. per 100 ml. Both patients were thus excreting considerably increased amounts of siderophilin in the urine, and had corresponding reciprocal changes in. the serum siderophilin level. These observations support the previously reported qualitative findings of Milliez et al. (J. Urol. méd. chir., 1959, 65, 248) in 30 patients with the nephrotic syndrome. The relationship of siderophilinuria to the anaemia in nephrotic patients is uncertain. It did not appear to contribute to the anaemia in the authors' first case, since there was no significant increase in haemoglobin concentration at a time when the urinary siderophilin content diminished and the serum level rose. Hewett A. Ellis

144. The Disappearance of Evans Blue Dye from the Blood in Normal and Nephrotic Subjects

P. J. H. Wyers and P. J. J. VAN MUNSTER. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 375-385, Sept., 1961. 2 figs., 24 refs.

The results of Evans (azovan) blue clearance studies in 5 patients with the nephrotic syndrome and in 7 healthy subjects are described in this paper from St. Radboud Hospital, Nijmegen, Netherlands. An intravenous injection of 0.3 to 0.8 mg. of the dye per kg. body weight was given and the urinary and serum concentrations were estimated serially at intervals over periods up to 35 days in the controls and of 9 to 22 days in the nephrotic patients. Concentrations of the dye were evaluated from measurements of the optical density of serum and urine before and after absorption of the dye on filter paper. Specimens were pretreated with a detergent to dissociate the albumin-dye complex. The 24-hour clearance values for azovan blue and albumin were calculated. Complete data for controls and patients are given in tables.

The urine of the nephrotic patients contained dye whereas that of the controls did not. In the former dye disappeared more rapidly from the blood than it did in the controls. Clearance of the dye did not equal that of albumin, and during the first one or two days after injection the 24-hour clearance of dye was less than that of albumin, whereas later it became greater. This dis-

crepancy could be explained in part by assuming that there was a transient absorption of the albumin—dye complex by the renal tubules with subsequent excretion of the dye into the urine at a time when the plasma dye concentration had diminished. The data show, however, that the "excess" of dye excreted after the first few days more than offset the "deficit" up to that time. This indicated that either the albumin—dye complex dissociated and albumin was selectively reabsorbed or the albumin was catabolized in the renal tubules. The authors favour the second explanation, since azovan blue is firmly bound to albumin.

145. Studies on the Pathogenesis of Nephrotic Edema, with Particular Emphasis upon Changes in Renal Hemodynamics and the Metabolism of Electrolyte and Proteins J. Metcoff and C. A. Janeway. *Journal of Pediatrics I. Pediat.* 58, 640-685, May, 1961. 19 figs., bibliography.

Some physiologic and biochemical observations on children with the nephrotic syndrome and on rats with an experimental nephrotic syndrome are summarized. Particular reference is made to renal function, including some estimates of renal thermodynamics associated with the secretion of potassium by the edematous nephrotic child. Electrolyte balances illustrate the accumulation and diuresis of nephrotic edema fluid with particular reference to the effect of sodium restriction and sodium loading in nephrotic children. The balance data suggest that edema is associated with a decreased intracellular potassium content, as well as an accumulation of Na and Cl extracellularly. Studies of the composition of muscle from a nephrotic child support this thesis. It is suggested that some of the discrepancies in estimating the retention and distribution of Na and Cl by balance measurements may be explained by correction for the retention of sodium, chloride, and water in skin and skeleton. A technique for such correction is illustrated. The skin appears to be the principal tissue reservoir of edema fluid according to such calculations, and some evidence for this is provided by analyses of skin from rats with the experimental nephrotic syndrome. In the edematous skins of these animals, sodium and chloride are retained in excess of their anticipated distribution in the extracellular and intracellular fluids. It is suggested that the "excess" sodium and chloride might be contained by loose electrostatic apposition to charged polar-end groups in the collagen fibril. Analytical data are given for "excess" Na and Cl of normal human skin, which are consistent with the above concept. Recent studies of cell composition of rats with an experimental nephrotic syndrome indicate a deficit of magnesium and organic phosphate as well as the accumulation of intracellular sodium and decreased concentration of potassium previously described.

An attempt has been made to integrate these observations with others taken from the available literature and other studies by our group upon plasma protein metabolism in the nephrotic syndrome, to construct a tentative, hypothetical schema for the pathogenesis of nephrotic edema.—[Authors' summary.]

Endocrinology

146. Pituitary and Adrenal Function during Administration of Small Doses of Corticosteroids

S. SHUSTER and I. A. WILLIAMS. Lancet [Lancet] 2, 674-678, Sept. 23, 1961. 6 figs., 30 refs.

It has been observed that daily doses of prednisolone as small as 5 mg., equivalent to about 25 mg. of cortisone, may be therapeutically effective in rheumatoid arthritis and idiopathic thrombocytopenic purpura; such a dose roughly equals the daily output of cortisol by the adrenal glands. On the assumption that doses of this magnitude are insufficient to suppress the pituitary (and so the adrenal) gland the therapeutic effect must be attributed to the administered steroid together with the normal adrenal secretion, that is, the sum of exogenous and endogenous steroid. This communication, from the Cardiff Royal Infirmary, records an attempt to find evidence of this additive effect.

In a first study, to 6 patients who had never previously taken corticosteroids, cortisone acetate was given orally in equal doses at 10 a.m. and 6 p.m., these being increased at intervals of 2 to 3 days [duration of administration not stated]. Estimation of the daily urinary output of 17-hydroxycorticosteroid metabolites before and during administration showed that in all patients this was increased with doses of 12.5 to 37.5 mg. of cortisone acetate daily. In a second study a group of 14 patients, 13 with rheumatoid arthritis and one with idiopathic thrombocytopenic purpura, receiving cortisone in a dosage of 25 to 100 mg. daily (or its equivalent in other corticosteroids), were compared with a control group of 5 patients convalescent from various non-endocrine diseases who had never taken corticosteroids and were given prednisolone, prednisone, methylprednisolone, triamcinolone, and dexamethasone respectively in doses equivalent to 25 mg. of cortisone. In both patients and controls adrenal and pituitary function were studied: (1) by the infusion of 25 Lu. of corticotrophin (ACTH) in 1 litre of 0.9% sodium chloride over 4 hours, blood being withdrawn for estimation of plasma cortisol concentration immediately before and during the infusion—this procedure gives maximum adrenal response in normal subjects; (2) by the intravenous injection of a bacterial pyrogen in a dose of 0.005 µg. per kg. body weight—this stimulates pituitary secretion of corticotrophin, the injection being followed in most cases by a rigor and a rise of temperature to 100 to 103° F. (37.8° to 39.4° C.) in 14 to 34 hours; as before, blood was withdrawn for plasma cortisol estimation immediately before and at intervals after the injection.

In patients taking 25 mg. of "cortisone equivalent" daily the response to corticotrophin and to pyrogen did not differ from that in the control patients, but in those taking 27.5 to 50 mg. of cortisone equivalent daily the responses were less, in varying degree, than those in the controls. It is concluded that the pituitary and adrenal

functions are normal in patients taking doses of steroid equivalent to 25 mg. of cortisone daily, but are depressed by higher doses. This conclusion thus confirms that the therapeutic efficacy of these small doses is due to summation of exogenous and endogenous steroid. In a discussion of the steroid withdrawal syndrome it is suggested that the corticosteroids are true drugs of addiction in that they lead to physical dependence on continued administration.

Kenneth Stone

PITUITARY GLAND

147. Immunoassay of Growth Hormone in Human Serum

R. M. EHRLICH and P. J. RANDLE. *Lancet* [Lancet] 2, 230-233, July 29, 1961. 3 figs., 21 refs.

In 1958 Read described an immunological method employing haemagglutination inhibition for the assay of human growth hormone (H.G.H.). From the University and Addenbrooke's Hospital, Cambridge, the present authors describe their own method, which is based on that of Read (in *Clinical Endocrinology* (ed. Astwood), New York, 1960) and report serum H.G.H. concentrations in health, acromegaly, hypopituitarism, and normal pregnancy and lactation.

H.G.H. was prepared from human pituitary glands by the method of Raben (Recent Progr. Hormone Res., 1959, 15, 71). Standard solutions were preserved withthiomersal (1:4,000) and stored in small lots of 0.3 mg. at -20° C. H.G.H. antiserum was prepared in rabbits by giving 3 subcutaneous injections at weekly intervals of 2 mg. of H.G.H. in a stable emulsion followed one week later by 1 mg. intravenously. H.G.H.-coated erythrocytes were prepared from defibrinated sheep's blood. For assay, complement was inactivated at 56° C. for 30 minutes and human serum samples were then absorbed with sheep erythrocytes until no agglutination was seen with the samples under the microscope. In principle the method depends upon the fact that agglutination of H.G.H.-coated erythrocytes by antiserum can be inhibited by the prior addition of H.G.H. to the serum. At a given concentration of antiserum a definite minimum quantity of H.G.H. is needed for inhibition of haemagglutination. This quantity is defined for both standard H.G.H. and serum in the assay at the end-point. The serum concentration of H.G.H. (in mug. per ml.) is then the product of the standard concentration of H.G.H. (in mug. per ml.) at the end-point and the dilution of serum at the end-point. The authors found that only one antigen in H.G.H. and only one antibody in antiserum was detected by agar-gel diffusion and immunoelectrophoresis. Using haemagglutination inhibition no cross-reaction was detected between antiserum and pure human corticotrophin or human serum albumin and

globulins. Since purified preparations of human thyroid-stimulating hormone, gonadotrophins, and prolactin are not at present available, it was not possible to test the antiserum for cross-reaction with these pituitary hormones.

The mean H.G.H. concentration in 24 samples of serum from normal subjects was $19.5 \pm 0.7 \,\mu g$, per 100 ml. In 6 of 12 acromegalics the values were greater than the upper limit of the normal range, the remaining 6 values being in the upper range of normal. H.G.H. was also estimated in sera from 10 hypopituitary patients. The values ranged from no detectable H.G.H. to 29 µg. per 100 ml., with a mean of $12.2\pm3.3 \,\mu g$. per 100 ml., which is significantly less than the mean normal value. The serum content of H.G.H. in successive trimesters of pregnancy did not differ from normal values, but in 10 patients studied 2 to 10 days post partum (when lactation had started) the serum H.G.H. level had increased to a mean of $36\pm4.4 \mu g$. per 100 ml. The antihormone activity of the antiserum was demonstrated by measuring its effect on weight gain induced in hypophysectomized rats by subcutaneous injections of H.G.H. The increase in weight over controls treated with saline was 15.8 ± 2.8 g., for H.G.H. alone, 5.1±2.5 g. for antiserum alone, and 5.8±2.4 g. for H.G.H.+antiserum.

The authors consider that their results confirm the claim of Read that haemagglutination inhibition may be used as the basis of an immunological assay for H.G.H. and for the assay of H.G.H. in serum. The findings appear to show that H.G.H. is present in the serum of normal subjects, but the present studies do not exclude the possibility that the biological effects of H.G.H. may be due to components in the serum which may be separated from the parent molecule in vivo. On the other hand since anti-H.G.H. serum has been shown to neutralize the biological effects of H.G.H. in hypophysectomized rats when H.G.H. and anti-H.G.H. serum are injected at separate sites it seems reasonable to conclude that the biologically active components of the H.G.H. molecule are estimated in this immunological assay.

148. Ocular Symptoms and Signs in Pitultary Tumours T. K. LYLE and P. CLOVER. Proceedings of the Royal Society of Medicine [Proc. roy. Soc. Med.] 54, 611-619, July, 1961. 13 figs., 9 refs.

John Lister

The importance of recognizing the ocular presentation of a pituitary tumour before the stage of fully developed bitemporal hemianopia is stressed. Examination of the visual fields is indicated in all cases of visual defect, however vague, when no cause of this is evident in the media or fundi. Patients are often unaware of their field defect until quite late in the course of the disease. Central vision likewise may not be affected early save in those cases where the field defect is of the scotopic type. When there is a reduction in the area of field overlap of the two eyes a patient who perhaps already has a latent divergence may complain of squint or of double vision. Ocular palsy due to compression of a nerve, often the oculomotor, is an occasional presentation.

The clinical records of 100 histologically proven cases of pituitary tumour, all of which were subjected to

operation at the National or King's College Hospitals, London, were examined. Of these, 94 had symptoms suggesting that the initial referral would be for an eye examination. An almost equally high number of patients considered that an ocular complaint was their first symptom. Of the field defects found, 79% were of the hemianopic type affecting the periphery and 15% were of the paracentral hemianopic scotomatous types with the periphery unaffected. All but one of the patients had a field defect of some type, perhaps demonstrable only with coloured targets, and some ways in which the various types of field defect presented themselves to the patient are described. Since marked visual defect is one of the most important indications for surgery in pituitary tumour this high incidence is not surprising in a series of surgically treated cases. In 56 cases pallor of one or other optic disk was observed. Alterations in the veins were sometimes found. Twenty patients had diplopia, of paretic_origin in 5, and 20 showed pupillary reaction changes, mostly attributed to the field defect. Of the 47 patients with headache, in 2 only was this of a type suggestive of an ocular origin. Pain around the eye was present in 13 cases. An accurate assessment of alterations in visual acuity was not possible in this series of patients. J. D. Abrams

THYROID GLAND

149. Studies on the Thyroid Activator of Hyperthyroid-

J. M. McKenzie. Journal of Clinical Endocrinology and Metabolism [J. clin. Endocr.] 21, 635-647, June, 1961. 1 fig., 26 refs.

It was shown by Adams (J. clin. Endocr., 1958, 18, 699) that when guinea-pigs or mice were injected with the serum of patients with hyperthyroidism a type of response occurred which differed from that which follows the administration of pituitary thyrotrophin in that its action was much more prolonged, suggesting that there may be in the blood of thyrotoxic patients a circulating substance which stimulates the thyroid gland. The presence of this second factor, for which the author proposes the term "thyroid activator of hyperthyroidism", has been sought in the sera of 101 patients with various forms of thyroid disorder, including 14 exophthalmic subjects without obvious thyroid dysfunction, at the Royal Victoria Hospital, Montreal.

The thyroid activator was found in 27 (79%) of 34 patients with active hyperthyroidism or with exophthalmos unassociated with apparent disturbance of thyroid function, in 21 (75%) of 28 euthyroid subjects who had previously suffered from hyperthyroidism, but in only one (4%) of 25 patients with no history of hyperthyroidism or exophthalmos (including 10 with myxoedema). The highest concentration of the activator substance was found most frequently in patients with severe exophthalmos or with hyperthyroidism prone to relapse after treatment.

Thyrotrophin-like responses were obtained only in patients with spontaneous myxoedema, except in one

case of hypothyroidism due to propylthiouracil. The thyroid activator was present in the serum of 3 patients who had been treated previously by section of the pituitary stalk, one who had undergone hypophysectomy, and many patients receiving thyroid extract. It was not found in the serum of one hyperthyroid woman whose thyroid function appeared, on the basis of ¹³¹I studies, to be limited to a solitary nodule, nor in the pituitary tissue obtained at necropsy on a patient whose serum during life contained the activator. On ultrafiltration of the serum the thyroid activator remained with the proteins and after separation of these by electrophoresis the activator was found in all protein fractions. In contrast, the thyrotrophin activity noted in sera from myxoedematous subjects is found in the y-globulin fraction alone. The possible implications of these various findings are discussed. H.-J. B. Galbraith

150. Effects of Guanethidine on Tri-iodothyronine-induced Hyperthyroidism in Man

T. E. GAFFNEY, E. BRAUNWALD, and R. L. KAHLER. New England Journal of Medicine [New Engl. J. Med.] 265, 16-20, July 6, 1961. 5 figs., 17 refs.

In this experimental study 4 normal subjects (2 women aged 18 and 40 and 2 men both aged 20) were observed closely at the National Heart Institute, Bethesda, Maryland, for nearly 3 months during which time they received a constant caloric intake and did not know whether they were being given a drug or a placebo. The study was divided into 5 periods. In the first the placebo was given for a control period of 9 days, after which triiodothyronine (T3) was started in doses of 50 μ g, per day and progressively increased "until significant elevations of the pulse and basal metabolic rates were produced". This dosage, which ranged from 225 to 350 μ g. per day, was continued throughout Periods 2, 3, and 4, each of which lasted 2 to 3 weeks. During Period 3 guanethidine was given in addition to T3, starting with 10 mg. daily and increasing "until the pulse rate was clearly affected", which occurred with doses varying from 20 to 50 mg. daily. The fifth period, when the placebo was again given, was for recovery.

The results were similar in all subjects. Sleeping and resting pulse rates rose by 35 to 55% in response to T3 alone, fell almost to the control level when guanethidine was added, rose again with T3 alone, and fell in Period 5 when it was stopped. Performance of a standard exercise in the supine position produced a nearly constant increase in pulse rate above the resting rate in all periods except the third (T3 and guanethidine), in which the rate showed much less increase. The basal metabolic rate (B.M.R.) rose by 25 to 50% above the control level with T3 alone, but after a week or more of taking guanethidine this increase was halved; the B.M.R. showed a renewed rise a week after guanethidine was stopped, with a return towards normal in the fifth period. Weight was constant in the control period, fell throughout Periods 2 to 4, and rose in Period 5, indicating that guanethidine did not influence the rate of loss of weight. [Fluid balance is not mentioned.] The serum cholesterol level fell by between 65 and 85 mg, per 100 ml, and remained low while T3 was given. Finger tremor increased with T3 alone, but lessened when guanethidine was added. The systolic blood pressure (supine and standing) was raised by T3 alone, but on the addition of guanethidine there was mild postural hypotension and the rise in supine systolic pressure was eliminated. It is suggested that these findings provide evidence that some of the signs of hyperthyroidism are due to an increased response to catechol amines.

G. C. R. Morris

PARATHYROID GLANDS

151. Hyperuricemia in Hyperparathyroidism D. H. MINTZ, J. J. CANARY, G. CARREON, and L. H. KYLE. New England Journal of Medicine [New Engl. J. Med.] 265, 112–115, July 20, 1961. 3 figs., 23 refs.

This paper from the Georgetown University School of Medicine, Washington, D.C., reports the investigation of 8 patients with hyperparathyroidism for associated hyperuricaemia or gout. The serum uric acid level and uric acid clearance rate were estimated together and changes in these values caused by removal of the parathyroid adenoma and subsequent administration of parathyroid hormone were noted. All the patients were maintained on a diet constant in its calcium and phosphorus content and within the known range of purine content.

Of the 5 male patients, 3 were found to be hyperuricaemic, as also was one of the 3 females, who also had a family history of gout. One of the hyperuricaemic men had a past history of acute intermittent gout. After the correction of the hyperparathyroidism the raised uric acid levels were unchanged, nor were any changes produced in them or the uric acid clearance rates during the administration of parathyroid hormone. The highest preoperative serum calcium levels were found in the hyperuricaemic patients and, even excluding one member with obvious renal disease, this group, despite increased filtered loads of uric acid, had the lowest levels of uric acid clearance. In view of the known damaging effects of long-continued hypercalcaemia on renal function it is suggested that abnormal renal function may be an important cause of hyperuricaemia in hyperparathyroidism.

The authors suggest that the high incidence of gout or a family history of the disease in 2 patients makes the screening of gouty subjects imperative if unsuspected cases of hyperparathyroidism are to be detected. This is especially important in those patients with recurrent ureteral stones. The converse—a search for hyperuricaemia in patients with primary hyperparathyroidism—is also obviously indicated.

J. Warwick Buckler

152. Calcium Intake in Patients with Primary Hyper-parathyroidism

C. E. DENT, B. V. HARTLAND, J. HICKS, and E. D. SYKES. *Lancet* [*Lancet*] 2, 336–338, Aug. 12, 1961. 2 figs., 8 refs.

The dietary histories over the previous 5 years of 51 patients who had been successfully operated upon for primary hyperparathyroidism at University College Hospital, London, were obtained, either by questionary or direct interview, to determine their calcium and phos-

phorus intake. The daily intake of each element was well within the normal range for all patients. Thus no support was provided for the hypothesis that a previous low calcium intake may be conducive to the development of parathyroid tumours. Similarly there was no difference in calcium intake between those patients with osteitis fibrosa and those without, suggesting a metabolic rather than a dietary cause for these two forms of primary hyperparathyroidism.

F. W. Chattaway

DIABETES MELLITUS

153. Serum Growth-Hormone Concentrations in Diabetes Mellitus

R. M. EHRLICH and P. J. RANDLE. Lancet [Lancet] 2, 233-237, July 29, 1961. 1 fig., 33 refs.

With the object of investigating the importance of growth hormone in the aetiology of diabetes and its complications the authors have applied the method of immunoassay of human growth hormone (H.G.H.) described in their previous paper [see Abstract 147] in determining the serum H.G.H. concentrations in a series of diabetics. The patients were classified as: untreated (no previous treatment with diet, insulin, or oral hypoglycaemic drugs); treated (with diet, insulin, or oral hypoglycaemic drugs) but without complications; patients with retinopathy; prediabetic patients; and pregnant diabetics.

In each of 7 untreated diabetics who were overweight and had not lost weight the serum H.G.H. content was elevated, the mean concentration being 41 μ g. per 100 ml. (normal 19.5 µg. per 100 ml.). Of 9 untreated patients who were not overweight, who had lost weight, and who had ketoacidosis, the serum H.G.H. content was elevated in one, but normal in the remaining 8. Of a further 9 untreated patients who had lost weight. who with one exception had not previously been overweight, and who required treatment with insulin, the serum H.G.H. content was elevated in 3 and normal in 6. Three of these patients had retinopathy and in 2 of these the serum H.G.H. level was raised. In all of 18 diabetics who had been treated for periods ranging from 2 days to 26 years and were clinically free of complications the serum H.G.H. concentration was within the normal range. In 8 of 17 patients with diabetic retinopathy the serum H.G.H! level was raised, but there was no correlation between serum H.G.H. level and duration of diabetes or its severity in terms either of need for treatment or grade of retinopathy. The serum H.G.H. level was elevated in 5 pregnant diabetics, at the upper limit of normal in one, and within the normal range in 2. The data were insufficient to enable the serum H.G.H. level to be correlated with the degree of control of diabetes or the birth weight of the baby. The serum concentration of H.G.H. in 5 prediabetics was normal.

Commenting on these findings, the authors suggest that in the untreated overweight diabetics the disease was probably precipitated by an increased serum level of H.G.H., presumably resulting from an increased secretion of the hormone. They consider that their finding.

that the serum H.G.H. level is usually normal in patients presenting with weight loss does not exclude the possibility that the diabetes was precipitated by an increased secretion of H.G.H. since patients in this group frequently pass through a phase of being overweight a year or so before the onset of the disease. While not suggesting that a raised serum H.G.H. level is responsible for diabetic retinopathy, they conclude that their finding of a raised level in 8 of 17 cases provides some theoretical basis for hypophysectomy in the treatment of the condition. The raised serum H.G.H. level in 5 of 8 pregnant diabetics, although it does not provide conclusive evidence, is in keeping with the suggestion that such an increase might be responsible for the increased birth weight and β -cell hypertrophy in the babies of diabetic mothers.

The authors do not conclude that an elevated serum H.G.H. concentration is necessarily the basic fault in diabetes. They consider that a basic inborn error of metabolism is made manifest and diabetes precipitated by an increased demand for insulin which may be brought about, for example, by an increased serum H.G.H. level through insulin antagonism.

John Lister

154. Treatment of Diabetic Retinopathy with Estrogens H. J. ROBERTS. Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.] 9, 655-685, Aug., 1961. Bibliography.

The value of oral and intravenous oestrogen therapy in the control and prevention of recurrent haemorrhage in patients with diabetic retinopathy was assessed in 9 such cases seen in private practice in Florida. The drug used was a conjugated equine oestrogen, "premarin", the oral dose being 0.3 to 1.25 mg. daily and the intravenous dose 20 mg.; male patients were given a dosage below that likely to produce gynaecomastia. Placebo tablets were also used as a control in several cases in which there was significant subjective improvement in vision. Progress was followed by clinical examination and standard tests for vision. Episodes of hypoglycaemia, which encourage further intra-ocular bleeding, were avoided by reducing the dose of insulin. Improvement was indicated by cessation of retinal haemorrhage and no further recurrence, objective visual improvement, or deterioration on withdrawing the oestrogen. Detailed histories are given of the 7 of the 9 patients who improved with oestrogen therapy over a period of 3 years; the remaining 2 patients had severe retinopathy, retinitis proliferans, and glomerulosclerosis. Intravenous oestrogen was also rapidly effective in controlling active bleeding. There were no toxic effects on the bone

The pathogenesis of diabetic retinopathy is reviewed. Venous stasis is followed by venous and capillary microaneurysms, and subsequent haemorrhages into the vitreous leads to retinitis proliferans. These changes are frequently, but not invariably, associated with diabetic nephropathy, and both may be aggravated by increased adrenocortical activity, for example, during infection or pregnancy. Pituitary factors are probably not important in the aetiology of diabetic vascular changes, although

hypophysectomy may result in improvement. Changes in intravascular osmotic relationships resulting in variations of intra-ocular pressure influence the retinal vascu-Jar degeneration, and alteration of the serum lipid and polysaccharide patterns is also a factor. Finally, a possible underlying immune reaction may be relevant. It has been shown that the haemostatic action of oestrogens is based on an increase in Factor V, decrease in plasma antithrombin activity, inhibition of fibrinolysis, and their effect on the capillary bed and on tissue mucopolysaccharides. The improvement in diabetic retinopathy with oestrogens may be due to an effect on serum lipids or on the whole metabolism or modification of pituitary and adrenal function. Additional uses of oestrogens in diabetic ocular complications include prevention of the haemorrhage of hyphema following cataract extraction and of retinitis proliferans and also possibly in pregnant diabetic women. Streptokinase, streptodornase, trypsin, and heparin may also be of value in diabetic retinopathy.

Although admitting that the present series is small, the author concludes that long-term oestrogen therapy is of value in preserving or improving vision in diabetic retinopathy without bleeding.

Gerald Sandler

155. Diabetic Gastric Atony: a Clinical Study
R. L. Wooten and T. W. Meriwether III. Journal of
the American Medical Association [J. Amer. med. Ass.]
176, 1082–1087, July 1, 1961. 5 figs., 14 refs.

Visceral neuropathy is a well recognized component of diabetes mellitus, but disturbance of gastric function has attracted little attention. Diabetic gastric atony presents a radiological picture like that which follows vagotomy. The stomach is atonic, showing evidence of retained food and fluid yet yielding to manual expression of barium through a normal pylorus. Accompanying clinical features are worsening of diabetic control, unexplained weight loss, vague abdominal complaints, and evidence of diabetic neuropathy elsewhere. Nine such cases are presented in this paper from the University of Tennessee College of Medicine and Baptist Memorial Hospital, Memphis, Tennessee, with the results of surgical intervention in 2 cases. One patient underwent pyloroplasty and the other subtotal gastric resection, neither with any benefit. Frequent feedings and good diabetic control with long-acting insulin seemed to be more effective. K. O. Black

156. "J"-Type Diabetes
J. A. Tulloch and D. MacIntosh. Lancet [Lancet] 2, 119-121, July 15, 1961. 11 refs.

In 1955 Hugh-Jones (Lancet, 2, 891; Abstr. Wld Med., 1956, 19, 384) reviewed the clinical types of diabetes that were encountered at the University College Hospital of the West Indies and found that 6% of cases could not be fitted easily into the usually recognized "insulin-deficient" and "lipoplethoric" types. Typically, these patients were under 40 years of age, underweight at onset of their diabetes, and relatively resistant to insulin, requiring over 80 units daily but showing little tendency to go into ketosis. Subsequent to this publication cases

of this type (Type "J") have been widely reported, mostly from underdeveloped parts of the world.

The present authors have made a further study of the 13 cases reported by Hugh-Jones and a further 11 cases fulfilling the same criteria seen at the University College Hospital of the West Indies. Observation of these patients for a period of 3 to 8 years showed that their progress was extremely varied and covered the usual range of diabetic behaviour rather than conforming to a consistent pattern. Eight of the patients had shown evidence of ketosis, 7 no longer required large doses of insulin, though 3 still required over 80 units daily, and 18 of them had increased in weight, some of them by a large amount. At least 10 of them no longer fulfilled the criteria for "J"-type diabetes.

A number of special investigations were carried out on some of these patients and the authors' conclusions are that there is no special "J"-type diabetes, but that patients falling into this clinical pattern at some stage in their diabetic career are really patients with "lipoplethoric" diabetes who have been poorly controlled.

[A review of cases in any diabetic clinic will reveal cases that fulfill the criteria for "J"-type diabetes at some time. The abstracter found that 3% of cases seen at a diabetic clinic in Great Britain met these criteria.]

T. D. Kellock

157. Symptoms of Mucoviscidosis in Diabetes Mellitus. (Mucoviscidosis-Symptome beim Diabetes mellitus) B. Koch, W. Lehmann, W. Rick, and W. Gumbel. Deutsche medizinische Wochenschrift [Disch. med. Wschr.] 86, 1433–1438, July 28, 1961. 6 figs., 27 refs.

This study, reported from the University of Giessen and the University Institute for Human Genetics, Kiel, sought to establish the genetic relationship between diabetes mellitus and mucoviscidosis. Of 37 of the 72 diabetic patients investigated in whom onset of the disease occurred before the age of 35, two-fifths showed a raised sodium concentration in the sweat and a lowered carboxy-peptidase level in the duodenal juice, while in a further two-fifths there were signs of lowered pancreatic enzyme activity. On the other hand, among the remaining 35 diabetics, with onset after the age of 35, only 2 showed some signs of mucoviscidosis.

Further investigations were carried out on 73 blood relations of the patients with diabetes and mucoviscidosis. In 32 of these no signs of either disorder were discovered, 20 had frank diabetes (or a diabetic blood sugar curve) and also showed signs of mucoviscidosis, while the other 21 exhibited signs of mucoviscidosis, but no evidence of diabetes. Further studies of the family histories brought to light numerous cases of undoubted diabetes and/or mucoviscidosis. The genetic implications of these findings are discussed.

H. F. Reichenfeld

158. Gastric Function in Diabetes Mellitus: a Clinical and Experimental Study with Special Reference to Gastric Secretion of Acid. [Monograph, in English]

G. DOTEVALL. Acta medica Scandinapica [Acta med. scand.] 170, Suppl. 368, 1-36, 1961. 2 figs., bibliography.

he Rheumatic Diseases

Arthritis Urica and Increased Erythropolesis A. NORDØY. Journal of the Oslo City Hospitals [J. Oslo Cy Hosp.] 11, 141-150, July-Aug., 1961. 4 figs., 18 refs.

This paper from Aker Hospital, Oslo, records 6 cases of anaemia associated with manifestations of gout. In 4 cases haemorrhage from the gastro-intestinal tract was followed several days later by joint symptoms, mostly in a large toe, with a serum uric acid level between 8 and 9 mg. per 100 ml., the normal upper limit by the method used being 7.5 mg. per 100 ml. Another patient, with valvular heart disease and recurrent epistaxis, had a haemoglobin level of 55% and gouty arthritis of several joints on admission. The sixth patient had iron-deficiency anaemia and a haemoglobin level of 56%; he developed acute gout after one week of iron medication. All 6 patients had a past history of attacks of gout.

The author considers that a reticulocyte response , coincides with increased uric acid excretion and a raised serum uric acid level. This condition, in a suitably predisposed individual, may then lead to an attack of gout. G. Loewi

1961. 4 figs., 9 refs.

ACUTE RHEUMATISM

The Radiological Picture of Rheumatic Pneumonia in Children. (Рентгеновская картина при ревматических пневмониях у детей) N. A. PANOV. Педиатрия [Pediatrija] 40, 16-21, Aug.,

In the author's opinion rheumatic pneumonia must be regarded as a hyperergic reaction to rheumatism in children. The early lesions are localized to the small peripheral vessels and in the chest radiograph appear as a coarse reticulation of the lungs with increased density at the hila. At a later stage the process involves the alveolar structure, with desquamation of the epithelium and formation of a hyaline membrane, while the alveoli are found to contain a sero-fibrino-haemorrhagic exudate. In this phase the radiograph shows numerous small foci of opacity which, however, differ from those of miliary tuberculosis in being confined to the deeper layers of the lung; these foci rapidly fuse to form dense rounded shadows with eroded and uneven contours. One characteristic of these appearances is the rapid changes in their distribution, the foci clearing up in one area and forming in another, but leaving as a rule the apices, bases, and lateral areas of the lung clear. This sharp distinction between the involved hilar areas and the uninvolved peripheral areas (often giving the shadow the appearance of a butterfly with outstretched wings) is diagnostic of rheumatic pneumonia and distinguishes it from other pulmonary complications, for example, interstitial pneumonia or simple pulmonary congestion due to cardiac failure.

Extensive pulmonary changes of the above type are compatible with a favourable outcome, but death may ensue if the carditis is severe. Radiology is of great value in the differential diagnosis of this condition from other respiratory or circulatory complications of rheumatism and also in indicating the best line of treatment.

L. Firman-Edwards

161. Changes in the Peripheral Nervous System in Acute Rheumatism in Children and Adolescents. (Изменения в периферической нервной системе при ревматизме у детей и подростков)

G. M. Bekker. Педиатрия [Pediatrija] 40, 28-32,

Aug., 1961. 4 figs., 21 refs.

That neuritis and polyneuritis occur in rheumatic children is well established. The complication of neuritis in an adolescent with rheumatism was first described by Freud in 1886, and Model and Simson reported the finding of peripheral nerve lesions in 30 out of 177 rheumatic children. The present author has investigated in detail the peripheral nervous system of 5 patients aged 9 to 17 years who died of rheumatism, one boy of 12 dying in his first attack, the others after repeated recrudescences; none had complained of symptoms of nerve involvement. The spinal ganglia at all levels, the brachial and lumbar plexuses, and the major nerve trunks of the upper and lower limbs were subjected to careful histological examination.

· In the cells of the spinal ganglia total or central chromatolysis was constantly present in some, accompanied by swelling of the body and eccentricity of the nucleus; much rarer was shrivelling of the nerve cells. Sometimes the former changes had led to death of the cell, and in these cases there was considerable proliferation of satellites, the latter in fact sometimes taking place even round unchanged cells. In the axis cylinders thickenings, and more rarely fragmentation, appeared, especially in the large and medium sized medullated fibres, which are usually regarded as afferent. The myelin was degenerated and broken up into droplets. In no case, however, was Wallerian degeneration observed. Alongside these dystrophic changes compensatory processes were evident, such as regeneration of fibres, hypertrophy of neurones and of accessory branchings ending in thickenings of various shapes and sizes, and "neurosymplastic" formation. This type of change was maximal in the lumbar spinal ganglia.

It is concluded that rheumatism is a disease in which the primary attack is on connective tissue, including that of the peripheral nerves or of any other organ. Thus acid mucopolysaccharides were demonstrated in the perineuronic and ganglionic connective tissue by Hall's and Macmanus's stains, while incubation with hyaluronidase increased the intensity of staining by these methods, proving the true nature of the deposit. Typical Aschoff nodes were not found in any of the cases, but nodes composed of histiocytes; fibroblasts, and lymphoid cells were often seen. There is thus evidence that the peripheral nervous system may be frequently involved in the rheumatic process, though there may be no clinical or neurological symptoms and signs of such involvement.

L. Firman-Edwards

162. The Urinary Content of Amino-acids in Children with Rheumatic Fever. (Содержание аминокислот в моче у детей, больных ревматизмом)

E. Č. Novikova and N. A. Ткоцкаја. Педиатрия [Pediatrija] 40, 37-41, Aug., 1961. 2 figs., 10 refs.

In the blood of the child with rheumatic fever, besides changes in the protein fractions, glycoproteins, and fibrinogen content, there is accumulation of mucoproteins, the protein fraction of which has been shown to be rich in tyrosine. This disturbance of protein metabolism involves not only qualitative changes in the protein fractions, but also the synthesis of tyrosine, leading to the appearance in the urine of this amino-acid and of its incompletely oxidized derivatives.

In the present investigation the urinary amino-acid content was estimated by ascending chromatography in 30 children with rheumatic fever who were given a standard diet supplying 3,017 Cal. per day and containing a normal protein content. Of these patients, 19 were suffering from the disease in the acute phase, while 11 had had repeated recrudescences. All had in the urine the following amino-acids: histidine, alanine, arginine, serine and glycine, glutamic acid and trionine, tyrosine, methionine and valine, 'phenylalanine and iso-leucine, and asparaginic acid. (Some of these had to be grouped in this way because the corresponding stains in the chromatogram were superimposed). Nearly all the children had free asparaginic acid in the urine, although it has been stated by many authorities that this substance is usually excreted in a combined form. In all the 19 acute cases the level of amino-acids (especially that of serine and glycine) was raised at the start of the attack; in 6 it declined as the disease subsided, while in 13 it rose at first and then fell as the clinical state improved (with the exception of one patient in whom the level remained above the initial value after 3 months). Of the 11 recurrent cases, however, only 2 followed this pattern, while 7 had a low urinary amino-acid content, although there was a certain correspondence between the levels of certain amino-acids and the clinical course of the disease. All the children in the recurrent group had some degree of cardiac failure. It is suggested that possibly the cardiac failure may disturb the assimilation of aminoacids from the gastro-intestinal tract. Of the 19 children in the first group, however, 10 had mitral incompetence, though none were in acute congestive failure.

L. Firman-Edwards

163. On the Prognosis and Natural History of Acute Rheumatic Fever and Rheumatic Heart Disease: a Study Based upon a 25-Year Material in a Swedish Town Served by a Single Hospital. [Monograph, in English]

P. HALL. Acta medica Scandinavica [Acta-med. scand.] 169, Suppl. 362, 1-122, 1961. 42 figs., bibliography.

CHRONIC RHEUMATISM

164. Hereditary Factors in Rheumatoid Arthritis and Ankylosing Spondylitis

J. J. DE BLÉCOURT, A. POLMAN, and T. DE BLÉCOURT-MEINDERSMA. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 215–223, Sept., 1961. 19 refs.

This study, reported from the University of Groningen, Netherlands, was carried out on a random series of 100 cases of rheumatoid arthritis (R.A.), 100 cases of ankylosing spondylitis (A.S.), 100 healthy subjects, and their relatives; the ages of the patients and control subjects ranged from 25 to 45 (mean 37) years and both sexes were represented in approximately equal numbers. Of 8,529 accessible relatives, 7,405 (86.8%) were interviewed and examined by the same specially trained physician, only those under the age of 15 being omitted. These included 2,486 relatives of the patients with R.A., 2,478 of those with A.S., and 2,441 relatives of the control subjects; besides members of the proband's immediate family, relatives included grandfathers and grandmothers, uncles and aunts, and also male and female cousins.

Among the relatives of patients with R.A. there were 58 cases of R.A. (42 in females and 16 in males), while in the control group 20 cases of R.A. were discovered (15 in females and 5 in males). Among the relatives of those with A.S. there were 45 cases (1.8%) of this disease, 30 (2.45%) in males and 15 (1.2%) in females; in the control group, only 2-cases of A.S. were found (0.08% of all relatives or 0.17% of male relatives). On the basis of these results it is suggested that both R.A. and A.S. involvé a non-sex-linked dominant hereditary mechanism with differences in penetrance between males and females. In a statistical appendix to the paper it is pointed out that both R.A. and A.S. are characterized by familial occurrence, but whereas families of R.A. patients show no increased occurrence of spondylitis; those of A.S. patients have more rheumatoid arthritis. It was calculated that about one-third of all Dutch families are affected by rheumatoid arthritis.

D. Preiskel

165. Panchondritis Rheumatica. (Zur Panchondritis rheumatica)

W. STROBEL and G. SEIFERT. Zeitschrift für Rheumaforschung [Z. Rheumaforsch.] 20, 247-256, Aug., 1961. 9 figs., 18 refs.

From the University of Münster, Westphalia, the authors describe a case of polychondritis in a 49-year-old woman. Her first symptom was dyspnoea, which was found to be due to stenosing laryngitis. Next, the external ear became inflamed and later episcleritis and conjunctivitis appeared. The patient became febrile and the other ear and then the nose were involved. Iridocyclitis and some degree of arthritis of the knees appeared and she became deaf. There was dyspnoea, with expiratory narrowing of the trachea and stridor. The external parts of both ears became flabby and the lower part of the nose collapsed. Laboratory investigation showed a raised leucocyte count and some elevation of the anti-

streptolysin titre, but the Rose-Waaler and latex tests and blood cultures all gave negative results. The serum levels of α - and γ -globulin fractions, fibrinogen, and alkaline phosphatase were all raised.

Treatment with 80 mg. of prednisone per day resulted in a recession of the inflammatory features and the stridor, but when dosage was reduced to a maintenance level of 35 mg. daily tracheotomy became necessary. The patient died shortly afterwards of pulmonary embolism. Necropsy revealed severe narrowing of the trachea and bronchi, with extensive loss of cartilage and replacement by granulation tissue. There was perichondritis and fibrosis with some new bone formation; the chondrocytes were partly swollen and partly disintegrated. Changes in the larynx, nose, and ear were similar, with some ossification in the cartilage, while those in costal and articular cartilage were of the same nature but less severe.

G. Loewi

166. The Diagnosis and Course of Rheumatoid Arthritis and Benign Aseptic Arthritis in Children. [In English] B. Hellström. Acta paediatrica [Acta paediat. (Uppsala)] 50, 529-544, Sept., 1961. 6 figs., 36 refs.

The author studied the nature and course of arthritis of non-septic origin in children admitted to 4 Stockholm hospitals from 1952 to 1957. His aim was to work out an evaluation of symptoms which would enable rheumatoid arthritis at an early age to be distinguished from the benign forms of aseptic arthritis. Patients with a shorter duration of arthritis than 3 weeks and those with allergic purpura, ulcerative colitis, leukaemia, or rheumatic fever were excluded from the study. This left a total of 91 patients identified from the hospital records, and of these, 87 were re-examined by the author and 3 by other physicians.

It was found that the cases could be classified into one group of rheumatoid arthritis (R.A.) according to accepted criteria and another group of benign aseptic arthritis (B.A.A.) which differed from the former in many respects. Major criteria for the diagnosis of R.A. included an arthritis of at least 6 weeks' duration, multiple involvement of joints, typical x-ray and serological changes, and confirmation by biopsy. Minor criteria were the continuous involvement of a single joint for 3 months, morning stiffness, subcutaneous nodules, erythema multiforme, and ophthalmic lesions. Two major criteria, or 1 major and 2 minor, were necessary for the diagnosis of R.A. This placed 48 cases in the R.A. group and 39 in the B.A.A. group. It was found that in the matters of heredity, sex incidence, preceding infection, incidence of trauma to the affected joint, and articular onset there was no significant difference between the two groups. Abnormal electrocardiographic findings were recorded in 4 cases of R.A., but the author admits that electrocardiography was not performed in every case, so that cardiac lesions were probably much commoner in this group. Ophthalmic lesions, including iritis, chorioiditis, and episcleritis, occurred in 6 of the R.A. group, but in none of the B.A.A. group. Typically, there was only a single comparatively brief bout of activity in the B.A.A. group, whereas in the R.A. group the period of activity was prolonged and often recurrent. In 11 cases of R.A. activity persisted up to 7 years, whereas there were only 2 relapses after a maximum of 2 years in the B.A.A. group. Half the R.A. group showed residual defects as against only one patient in the B.A.A. group.

The author considers that the classification may be of use in children because it allows the physician to arrive at a diagnosis sooner and puts him in a better position to predict the course of the disease in an individual case.

William Hughes

167. Investigation of the Rheumatoid Factor by the Rapid Latex Test and by Ultracentrifugation in Rheumatoid Arthritis. (Der Nachweis des Rheumafaktors durch den Latex-Schnelltest und durch Ultrazentrifugenuntersuchung bei der primärchronischen Polyarthritis)
D. KOCH and H. ODENTHAL. Deutsche medizinische Wochenschrift [Disch. med. Wschr.] 86, 1767-1768, Sept.

15, 1961, 11 refs.

In performing the rapid latex test serum diluted with buffer is added to a latex suspension containing y globulin, a positive reaction being recorded when there is agglutination of the latex particles. The reliability of this test was compared at the Medical Academy, Düsseldorf, with that of the ultracentrifuged sedimentation test in detecting the rheumatoid factor in rheumatoid and non-rheumatoid sera. The rapid latex test was found to be highly sensitive, giving a positive result in 35 (95%) of 37 sera from patients with rheumatoid arthritis, but it was only moderately specific, since it gave a positive result in 25% of non-rheumatoid sera (71 samples). On the other hand, the ultracentrifuge sedimentation test was found to be highly specific, giving no false positive results in non-rheumatoid sera, but was not very sensitive since in only 46% of the rheumatoid arthritis sera did it reveal the characteristic pattern associated with this G. W. Csonka disease.

168. Digital Arteritis in Rheumatoid Disease

J. T. Scott, D. O. Hourihane, F. H. Doyle, R. E. Steiner, J. W. Laws, A. St. J. Dixon, and E. G. L. Bywaters. *Annals of the Rheumatic Diseases [Ann. rheum. Dis.]* 20, 224–234, Sept., 1961. 13 figs., 16 refs.

In this study of digital arteritis in selected patients with rheumatoid arthritis, carried out at the Canadian Red Cross Memorial Hospital, Taplow, Bucks, the lesions were demonstrated by brachial arteriography, 10 ml. of 45% "hypaque" being injected rapidly into the brachial artery at the elbow. In most cases a local anaesthetic was given and a rapid series of films were exposed at one-second intervals for 8 seconds. The arteriograms were found to be abnormal in 10 adult patients in whom there was some suspicion of digital arterial disease, but were normal in 2 others with rheumatoid arthritis in an early stage in whom there was no indication of arteritis. In yet another case it was possible to carry out arteriography and histological examination post mortem.

Radiologically, the lesions showed irregularity and narrowing or obliteration of the arterial lumen. The

changes, which are not specific, may occur in patients with clinically normal hands and normal reactive hyperaemia. All the patients were over the age of 40 and 9 were male and 2 female. The differential agglutination test gave a positive result in all, and 9 out of 11 patients had subcutaneous nodules. No L.E. cells were found. Peripheral neuritis was present in 7 patients and in all but one of these was associated with ischaemic digital skin lesions. The relationship to steroid administration is uncertain, since 2 of the patients had received no steroids and in a 3rd there was evidence of digital ischaemia before steroids were given. The mechanism involved is also obscure, but the direct role of the rheumatoid factor (binding to blood elements and vessel wall) is suggested as a possibility. D. Preiskel

COLLAGEN DISEASES

169. Simple Determination of the L.E. Factor. Loose Body Test and Nucleus Agglutination Inhibition Test F. VAN SOEREN. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 281–288, Sept., 1961. 2 figs., 26 refs.

When isolated leucocyte nuclei (prepared by treating leucocytes with distilled water) are mixed with normal serum they form a nucleoprotein clot which rapidly settles, leaving clear supernatant serum. When isolated nuclei are mixed with serum from a case of systemic lupus erythematosus L.E. bodies are formed which can be identified microscopically (the loose body test) or by the persistent turbidity of the serum (nucleus agglutination inhibition test). These tests can be made quantitative if serial dilutions of the serum are used.

Working at the University of Amsterdam the author has evaluated these tests on 800 sera. The loose body test gave many more positive results than did parallel L.E.-cell tests in systemic lupus erythematosus as well as in other diseases. The nucleus agglutination inhibition test gave similar results to the L.E.-cell test except in 208 cases of rheumatoid arthritis, in which the former test gave 17 and the latter only 10 positive results.

The author considers that these tests are more sensitive than the L.E.-cell test because they are independent of phagocytosis, which is sometimes inhibited in systemic lupus erythematosus.

M. Wilkinson

170. Anaemia Due to Systemic Lupus Erythematosus.

O. HEINIVAARA and A. EISALO. Annales medicinae internae Fenniae [Ann. Med. intern. Fenn.] 50, 73=81, 1961. 18 refs.

The authors, working at the University of Helsinki, have investigated the blood picture in 36 women and 7 men with systemic lupus erythematosus, the observations being made while the disease was active and still untreated; the series was unselected except that patients with a history of recent haemorrhage were excluded. In 32 of the 43 patients the haemoglobin value was less than 11 g. per 100 ml. The anaemia was normocytic and hypochromic, and the mean corpuscular haemoglobin concentration was above 29% in only one of

10 patients in whom it was determined. The leucocyte count was below 4,000 per c. mm. in 8 patients, while the proportion of monocytes was over 10% in 18 patients and these cells often showed abnormal morphology. The serum iron level was low (less than 60 μ g. per 100 ml.) in 15 out of 24 patients, but there was no evidence that the serum level of the iron-binding protein siderophilin (transferrin) was lowered.

A study of the bone marrow in 24 patients showed hypocellularity, with increased quantities of fat, normal erythropoeisis, and proliferation of the reticulum cells. Half the patients showed some increase in plasma cells. Hyperplasia and reticulocytosis, suggestive of haemolytic anaemia, were not seen. The anaemia did not respond to administration of iron, but appeared to improve during remissions of the lupus erythematosus, whether these were spontaneous or induced by treatment with cortisone.

The authors conclude that toxic factors are probably important in causing the anaemia in patients with lupus erythematosus.

G. L. Asherson

171. Studies of Relatives of Patients with Systemic Lupus Erythematosus

O. G. MORTEO, E. C. FRANKLIN, C. McEWEN, J. PHY-THYON, and M. TANNER. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 356–363, Aug., 1961. 34 refs.

This paper from the New York University School of Medicine and Bellevue Hospital Center, New York, presents data obtained from clinical and laboratory examinations of 44 relatives of 19 patients suffering from systemic lupus erythematosus (S.L.E.). (The complete report on the patients is to be published separately.) In addition, 46 subjects forming a control group matched and comparable in age and sex were examined by the same methods.

Clinically, 5 relatives of 4 different patients had evidence of rheumatoid disease. In the laboratory studies 16 of the 44 relatives gave positive reactions for the rheumatoid factor; 2 of the 16 had rheumatoid arthritis and 14 were asymptomatic. Eight relatives had hyperglobulinaemia as estimated by the zinc turbidity and electrophoretic methods. Only one relative presented a clinical picture compatible with S.L.E. and had a positive L.E. cell preparation, although antinuclear antibodies were demonstrated in the blood of 6 by the fluorescent technique. Five relatives provided biological false positive reactions to serological tests for syphilis.

In summary, it was found that three-quarters of the propositi had at least one relative with some unusual laboratory finding and one-sixth had at least one close relative with clinical evidence of collagen disease, the most marked finding being the presence of rheumatoid factor in more than one-third of the relatives. The authors suggest that "the results offer additional evidence that S.L.E. and rheumatoid arthritis are closely related diseases, and the findings are consistent with the hypothesis that they may, in some as yet unknown manner, reflect a genetically determined abnormality in the immune response and the synthesis of gammaglobulins".

Harry Coke

Neurology and Neurosurgery

172. Electro-clinical Correlation in Temporal Lobe Epilepsy with Emphasis on Inter-areal Analysis of the Temporal Lobe

J. R. Hughes and R. E. Schlagenhauff. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 333-339, June, 1961. 14 refs.

For this study, reported from the University of Buffalo Medical School, New York, the authors selected 100 cases of temporal-lobe epilepsy in which focal discharges in the electroencephalogram (EEG) were limited to the anterior, mid, or posterior temporal areas of either one or both hemispheres. Both waking and sleep records were obtained and the number of independent discharges was counted in each of the three temporal areas on either side. In 55 of these cases the epileptiform discharges appeared only during sleep. These discharges were unitemporal in 37 and bitemporal in 63 cases; of this latter. group of patients, the majority showed predominantly left-sided abnormalities, and they also tended to have a longer history of seizures—a mean period of 13.7 years compared with 9.7 years in the unitemporal cases. An anterior temporal location was most common in the unilateral cases, whereas in the bilateral cases a midtemporal distribution was somewhat more frequent.

Attacks of grand mal and of automatism were relatively more common in cases with anterior temporal foci, while behaviour disorders, particularly aggression, were more often associated with mid-temporal foci. Ictal vertigo, "autonomic changes", "strange ideas, memory flashbacks, mood changes, and strange urges" showed a close association with mid-temporal discharges, which the authors consider often have their origin in the hippocampal region. No clinical correlates could be established with the laterality of the foci. The authors conclude that in the "average" unitemporal case bilateral discharges are likely to develop after 14 years of seizures and point out that if this can be confirmed it may have an important bearing on the timing of temporal lobectomy.

L. G. Kiloh

173. The Electroencephalographic Findings in Acute Intermittent Porphyria

R. S. Dow. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 425-437, June, 1961. 8 figs., 21 refs.

The electroencephalographic (EEG) findings in 3 cases of acute intermittent porphyria investigated at the Good Samaritan Hospital, Portland, Oregon, are discussed, following an [incomplete] review of the relevant literature. The essential abnormality in all 3 cases was an excess of diffuse slow activity, the frequency and quantity of which varied according to the severity of the attack. In the more severely disturbed patients, delta activity as low as 1 c.p.s. was evident; this might be irregular or

synchronous, and even asymmetrical on occasions. In 2 of the cases convulsions were a prominent clinical feature, and in one of them unilateral sharp-wave activity occurred [though the tracing illustrated is far from convincing]. The biochemical changes responsible for the EEG changes are not understood, but it is considered unlikely that they are due to circulating porphyrins.

L. G. Kiloh

174. 'Prognosis in Bell's Palsy

W. B. MATTHEWS. British Medical Journal [Brit. med. J.] 2, 215–217, July 22, 1961. 8 refs.

According to the author of this paper from the Derbyshire Royal Infirmary, Derby, "the rate of complete recovery in Bell's palsy is often stated to be 80 to 85%, without further support, even by authors whose own results by no means approach this level". In order to establish the prognosis in early cases 155 consecutive patients with Bell's palsy were studied. Of 22 patients seen within 2 days of the onset of facial weakness, 16 (73%) recovered completely. The recovery rate in 45 patients seen within 6 days of onset was 60%, and complete recovery was observed in 54% of 125 cases seen within 2 weeks of onset and in 48% of 153 cases seen within 3 months of onset.

The author confirms the relatively bad prognostic significance of advancing years, a complete palsy, and herpes zoster. In 118 cases seen within 2 weeks of onset a recovery rate of 69% (44 out of 64) was obtained in patients under 40 years of age compared with one of 44% (24 out of 54) in patients over 40. In 153 cases seen within 3 months of onset complete recovery was observed in only 25 (30.5%) of 82 patients with a complete palsy compared with 49 (69%) of 71 with a partial palsy. Only one of 9 patients with herpes zoster recovered completely.

A. G. Freeman

175. Late Causes of Death and Life Expectancy in Paraplegia

D. J. Breithaupt, A. T. Jousse, and M. Wynn-Jones. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 73-77, July 8, 1961. 4 figs., 10 refs.

The authors have studied the late complications and the incidence of death among 599 cases of traumatic paraplegia treated at three hospitals in Toronto between 1945 and 1958, the information being obtained by a questionary and a detailed follow-up. The total number of deaths was 94 (15.7%). The mortality in the paraplegic group was 7 times greater than that in the general population at the age of 25 years, falling to 13 times greater at the age of 65. The authors conclude that "the death rate of carefully treated paraplegics is three times that of the total population". Genitourinary sepsis accounted for up to 50% of the fatalities.

I. Ansell

BRAIN AND MENINGES

176. Cortico-callosal Lesions in Alcoholism. (Lésions cortico-calleuses de l'éthylisme)

J. Delay, S. Brion, R. Escourolle and A. Sanchez. World Neurology [Wld Neurol.] 2, 662-671, Aug., 1961. 2 figs., 21 refs.

In alcoholic encephalopathies spongy sclerosis of the third lamina of the cerebral cortex with macroglial reactions (laminar cortical sclerosis of Morel) and necrosis of the corpus callosum, especially anteriorly, with demyelinization and glial and macrophage reactions (Marchiafava-Bignami) sometimes occur and are frequently present together. Clinically, these changes are associated with progressive dementia, agitation, disturbance of consciousness often developing into coma, ataxia, tremor, dysarthria, hemiplegia, grasp reflexes, and apraxia. The picture resembles that of a frontal-lobe tumour. At the present time the relationship of these clinico-pathological changes to Wernicke's syndrome is not clear.

From the Clinique des Maladies Mentales et de l'Encéphale, Paris, the authors report an anatomical study of the brains of 5 chronic alcoholics showing both cortical and callosal lesions. (Lesions of the mammillary bodies were also present.) They compared 32 cases of isolated necrosis of the corpus callosum with 14 cases showing both necrosis of the corpus callosum and cortical sclerosis and 4 cases of pure cortical sclerosis. The necrosis of the corpus callosum is usually more massive and widespread when accompanied by cortical lesions than when occurring alone, but the two types of lesion are clearly related. The symptoms are similar in all these conditions, but are more intense when callosal and cortical lesions are combined. Cortico-callosal lesions are rarely found associated with the characteristics of Wernicke's encephalopathy, and the two conditions appear to be of different actiology.

R. Wyburn-Mason

177. Cerebral Hemispherectomy in the Treatment of Infantile Hemiplegia: Review of the Literature and Report of Two Cases. [In English]

H. H. WHITE. Confinia neurologica [Confin. neurol. (Basel)] 21, 1-50, 1961. 4 figs., bibliography.

178. Anglography in Acute Head Injuries.
D. O. HANCOCK. Lancet [Lancet] 2, 745-747, Sept. 30, 1961. 32 refs.

The investigation of acute head injuries by means of carotid angiography has up to now not been widely adopted in Great Britain, but this paper from the Frenchay Hospital, Bristol, points out that it has many advantages over the so-called "woodpecker operation" of multiple exploratory burr-holes in the management of severe head injuries with suspected intracranial haemorrhage.

The paper reviews 620 cases of head injury seen in a 10-year period. Angiography was carried out in 174 of these cases and the results are analysed. It is concluded that angiography was of definite value in 69% of the

cases in which it was used and it is implied that some patients may be lost through failure to use it.

[This is an important paper which should be read by all concerned in the management of head injuries, not only in neurosurgical centres, but in general hospitals where the majority of cases of head injury are seen and managed, often inadequately by modern standards. Cerebral angiography should no longer be regarded as the esoteric preserve of a few special centres, but should be common practice in all well equipped radiological departments in general hospitals.]

J. MacD. Holmes

179. Cerebral' Artery Occlusions in Children Due to Trauma to the Head and Neck: a Report of 6 Cases Verified by Cerebral Angiography

E. Frantzen, H. H. Jacobsen, and J. Therkelsen. *Neurology* [*Neurology* (*Minneap.*)] 11, 695-700, Aug., 1961. 3 figs., 18 refs.

Cerebral artery occlusions subsequent to trauma involving the head or neck developed in 6 patients aged 20 months to 14 years. On arteriography, occlusion of the internal carotid artery was found in 3 cases and occlusion of the middle cerebral artery in 3. Remission of symptoms was generally poor, and all patients showed residual symptoms.—[Authors' summary.]

180. "Completed Stroke" Due to Occlusive Cerebrovascular Disease: an Analysis of 409 Cases
E. S. GURDJIAN, D. W. LINDNER, W. G. HARDY, and

L. M. THOMAS. Neurology [Neurology (Minneap.)] 11, 724-733, Aug., 1961. 8 figs., 1 ref.

At the Grace and Detroit Memorial Hospitals, Detroit, Michigan, 409 patients were seen between July, 1956, and April, 1960, who were suffering from "completed '. This was defined as " a neurologic deficit due to occlusive cerebrovascular disease which may persist for hours or days". The patients' ages ranged from the 4th to the 9th decade, but 70% were in the age group 50 to 70 years. There were 258 males and 151 females. The examination of the patients included 4-vessel cerébral angiography which revealed abnormalities, that is, stenosis or occlusion of a large vessel, in rather more than one-half of the patients. One-half of the patients presented with a single stroke of sudden onset, in onethird the onset was described as "episodic", and in one-ninth the onset was progressive. Of the patients with episodic onset, 55% were found to have occlusive disease of the larger vessels in the neck and at the base of the brain. In two-thirds of the cases in which the angiographic findings were normal there was clinical evidence pointing to major focal neurological abnormalities. The clinical features associated with the various angiographic findings are described in outline.

The authors consider that in patients with reversible neurological deficits there is focal ischaemia of the brain which depends mainly upon the patency of the small cerebral vessels. Stenosis of a major proximal vessel is in many cases a very important factor in the production of focal ischaemia, but in other cases such a lesion seems to be of little consequence. Digital compression of the

carotid artery may be valuable in assessing the importance of these lesions.

Anticoagulant therapy is indicated in cases of episodic stroke when a diagnosis of disease of the small arteries is made after angiographic study. It is suggested that "the ideal candidate for endarterectomy is the patient who has (1) recurring or episodic focal neurologic abnormalities with periods of normalcy between attacks, (2) a normal electroencephalographic pattern, (3) a positive response to digital carotid artery compression on the side opposite the stenotic lesion, (4) clear cerebrospinal fluid, and (5) tolerance to digital carotid compression of the involved carotid artery".

Bernard Isaacs

181. The Electroencephalogram during Administration of 100% Oxygen and of 5% Carbon Dioxide in Patients with Cerebral Infarction

J. Potes and C. E. Wells. Neurology [Neurology (Minneap.)] 11, 738-741, Aug., 1961. 1 fig., 8 refs.

At Bellevue Hospital, New York, and the New York Hospital-Cornell Medical Center, a study was made of the influence of the administration of 5% carbon dioxide in oxygen and of 100% oxygen on the slow-wave activity present in the electroencephalogram of 36 patients with a clinical diagnosis of cerebral infarction. With 5% carbon dioxide a reduction of slow-wave activity was observed in 30 of 37 tests, while with 100% oxygen inhalation no significant change occurred. The authors feel that these findings point to the need for further controlled studies of the possible therapeutic value of inhalation of carbon dioxide in cerebral infarction.

Bernard Isaacs

182. The Fluorescein Dye Test of Circulation Time in Patients with Occlusive Disease of the Carotid Arterial System

R. W. HOLLENHORST and T. P. KEARNS. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 36, 457-465, Aug. 30 [received Oct.], 1961. 5 figs., 1 ref.

At the Mayo Clinic the circulation time in 28 patients thought to be suffering from cerebrovascular disease or from a circulatory anomaly was investigated by means of the fluorescein dye test, which measures the time taken for the blood to flow from an antecubital vein to the central retinal arteries. In performing it 5 ml. of 10% fluorescein dye is rapidly injected intravenously, while two observers, using ophthalmoscopes fitted with cobaltblue filters, time the arrival of the dye in the retina. In patients shown by arteriography to have a normal carotid arterial tree the arm-to-retina circulation time varied from 10 to 16 seconds (mean 13.3 seconds). In 6 of 10 patients with arteriographic evidence of unilateral stenotic or occlusive disease of the carotid tree the circulation time was greater on the affected side than on the normal side, the difference ranging from 1.5 to 7.8 seconds; in the other 4 patients there was no significant difference in time between the two sides. Of 6 patients considered clinically to have stenosis or occlusion of a carotid artery, who had not been investigated angiographically, only 2 showed a significant slowing of the circulation on the affected side.

All 28 patients in the series were also studied by ophthalmodynamometry, and the authors consider that the latter procedure is at present a more reliable indicator of disturbance in the carotid arterial system than is measurement of the circulation time.

Bernard Isaacs

183. Lung and Heart Complications of the Treatment of Hydrocephalus by Ventriculoauriculostomy

J. L. EMERY and H. B. HILTON. Surgery [Surgery] 50, 309-314, Aug., 1961. 2 figs., 19 refs.

Although the introduction of the Spitz-Holter valve as an aid to ventriculo-auriculostomy represented a further advance in the treatment of infantile hydrocephalus, it brought its own complications, such as pulmonary embolism, septicaemia, and clot formation in the superior vena cava and heart. In this paper from the Department of Pathology, Children's Hospital, Sheffield, the authors describe the pathological findings in 15 children (out of a total of over 100 subjected to the operation) who came to necropsy, having died at periods varying from 3 days to 26 months after ventriculo-auriculostomy. The findings are grouped under two headings: cardiac and pulmonary. In regard to the former group all cases showed fibrosis around the intra-auricular portion of the catheter. in 6 there was endocardial thrombosis in situ, and thrombotic occlusion of the great veins entering the right auricle had occurred in a further 6. As to the pulmonary sequelae, multiple pulmonary emboli were found in 14 of the 15 cases, with focal arteritis unassociated with obvious embolism in some, and formation of mycotic aneurysms on the pulmonary arteries in 7 others. In 2 cases the child had died suddenly from massive pulmonary thrombosis and in one other a progressive pulmonary haemosiderosis had been associated with severe anaemia. A comprehensive table of the post-mortem findings in each case is presented.

The authors speculate as to the cause of the thrombosis and suggest that infected spinal fluid (7-of the patients showed necropsy evidence of meningitis) or the reaction of the vessel wall to the "foreign" protein of the spinal fluid may be among the factors responsible. They stress the need to treat without delay pyrexial episodes and minimal chest signs occurring in patients subjected to ventriculo-auriculostomy, since such episodes should be regarded as due to acute bacterial endocarditis.

J. B. Foster

184. Drug Therapy in the Crises of Postencephalitic Parkinsonism

G. ONUAGULUCHI. Scottish Medical Journal [Scot. med. J.] 6, 368–375, Aug., 1961. 3 figs., 15 refs.

The author discusses the treatment of oculogyric crises and sweating crises in 11 patients with post-encephalitic Parkinsonism at Stobhill Hospital, Glasgow, Barbitone by mouth did not affect the natural course of the crises, but intravenous injection of 150 mg. and intramuscular injection of 50 mg. of sodium phenobarbitone was successful in stopping the crises within 10 to 20 minutes, although in some instances of very severe crisis a relapse occurred 60 to 90 minutes after administration of the drug

In prophylaxis, however, barbiturates were of little value, and a trial of sodium phenytoin prophylactically showed that while the drug altered the character of the crises, they were more prolonged and quite definitely more unpleasant to the patient.

N. S. Alcock

EPILEPSY

185. Treatment of Petit Mal with Ethosuximide K. W. G. Heathfield and E. C. O. Jewesbury. British Medical Journal [Brit. med. J.] 2, 565-567, Aug. 26, 1961. 4 refs.

The authors of this preliminary communication from the Whipps Cross and the Royal Northern Hospitals. London, describe the results of administration of ethosuximide in 50 patients suffering from petit mal. Almost all the patients had been treated with phenobarbitone, and 27 had also received troxidone, aloxidone, phensuximide, or amphetamine. Ethosuximide, which was prescribed in addition to the medication the patient was already receiving, was given in a dosage initially of 250 mg. (one capsule) 2 to 3 times a day, this being increased. if necessary, up to 6 capsules a day. The petit mal was successfully controlled in 27 patients; 21 remaining free from attacks for an average period of 10 months and 6 experiencing only occasional attacks (one a-month), usually precipitated by stress. In 7 cases ethosuximide was withdrawn gradually after 6 months' treatment without recurrence of petit mal attacks, the patients remaining free for 12 months.

Side-effects occurred in 17 patients, including 14 who were receiving 250 mg. 3 times a day. Apathy, depression, or drowsiness occurred in 8, nausea in 5, vomiting in 4, and dizziness and a transient stammer each in one patient. In 5 further patients apathy, nausea, or vomiting was observed when the dosage was increased to 4, 5, or 6 capsules a day, but the symptoms subsided when the dosage was reduced. In 4 cases the drug had to be withdrawn. No skin rashes were observed, but in some instances the polymorphonuclear leucocyte count was between 2,000 and 3,000 per c.mm. In 2 patients in whom leucopenia had developed during treatment with oxazolidine-dione compounds the polymorphonuclear leucocyte count increased after administration of ethosuximide began.

186. Clinical Evaluation of 1-Methyl-5:5-phenyl-ethylhydantoin in the Treatment of Epilepsy

S. LIVINGSTON, L. L. PAULI, I. KRAMER, and A. NAJMA-BADI. New England Journal of Medicine [New Engl. J. Med.] 265, 418-421, Aug. 31, 1961. 17 refs.

The results obtained with a new hydantoin, 1-methyl-5:5-phenylethylhydantoin, in the treatment of epilepsy in 89 patients who had been receiving the drug for 6 months or more are described in this paper from Johns Hopkins Hospital, Baltimore. Of the 89 patients, 56 were between 2 and 14 years of age and 33 were over 14 years; 59 had grand mal seizures, 10 had petit mal, and 20 had mixed seizures. The drug was given in a dosage of 100 mg. daily, increased by 50-mg. increments each

week until control was obtained or signs of intolerance developed. Other drugs had been tried in the treatment of 82 of the patients, but without appreciable benefit, despite maximum doses.

In 43 of the patients the seizures were completely controlled (6 to 24 months' treatment); in 16 there was 75% reduction in the number of seizures, and in 15 a 50% reduction. The remaining 15 patients failed to respond. Of the 59 patients with grand mal attacks, 51 were improved; of 10 with petit mal, 5 were improved, while in 3 the attacks were controlled; of 8 with psychomotor and grand mal epilepsy, 3 showed control of seizures and 4 were improved. Skin rashes developed in 4 patients 10 to 14 days after starting treatment. Ataxia occurred with large doses in 6 cases but disappeared when the dose was reduced. In a 3½-year-old boy nephrosis developed which cleared up when steroids were administered and the drug was discontinued. No haematopoietic or hepatic disorders were observed.

Commenting on the findings the authors consider that the best results were obtained in grand mal epilepsy. Of the patients with petit mal seizures who improved, 6 were children approaching adolescence and the improvement may have been spontaneous.

N. S. Alcock

187. Psychomotor Epilepsy in Childhood. Part III (Die psychomotorische Epilepsie im Kindesalter. III. Mitteilung)

A. MATTHES. Zeitschrift für Kinderheilkunde [Z. Kinderheilk.] 85, 668-685, 1961. 2 figs., 36 refs.

In this third part of a review of 135 cases of psychomotor epilepsy in childhood, carried out at the University Paediatric Clinic, Heidelberg, the author discusses aetiological factors, pathological anatomy and physiology, clinical course, and prognosis.

The aetiology was reasonably certain in 74 cases. Of the remaining 61 cases, 45 showed evidence of organic brain disease of undetermined origin; in only 16 could no evidence by obtained, from the history or special investigations, of organic disease of the brain. Of the 74 cases of certain aetiology, 36 resulted from birth trauma or intra-uterine brain damage, while 38 were the result of post-natal brain disease or injury. Heredity played no greater role in these cases than in other forms of epilepsy. Duration of the epileptic condition and the frequency of fits and factors influencing this are discussed, together with the association of grand mal with psychomotor epilepsy. Such an association was found in 32% of the cases, while in 46% the epilepsy was ushered in by a grand mal attack. The author divides his case material into three groups of psychomotor epilepsy on the basis of clinical and electroencephalographic features, and indicates the prognosis in the three groups respectively.

[This paper, together with the author's two preceding studies (Z. Kinderheilk., 1961, 85, 455 and 472; Abstr. Wld Med., 1961, 30, 482), represent the results of a very interesting and thorough investigation into psychomotor epilepsy in childhood and include a useful review of the literature on this subject.]

J. B. Stanton

Psychiatry

188. Two Generations of Broken Homes in the Genesis of Conduct and Behaviour Disorders in Childhood C. J. Wardle. British Medical Journal [Brit. med. J.] 2, 349-354, Aug. 5, 1961. 1 fig., 10 refs.

In an attempt to ascertain the role of an adverse home in the causation of behavioural abnormality in childhood 185 children (125 boys) aged 4 to 15 years attending the Brixton Child Guidance Clinic, London, over a one-year period were studied. Of these, 120 came from intact homes, but 12 of them had suffered at least 6 months' separation from their parents, while the remaining 65 came from broken homes; although 43 of these last were living with their natural mother, 17 of them had been separated from her for 6 months or more at some time.

The incidence of neurotic behaviour was significantly higher (46.7%) in those from intact homes than in those from broken homes (24.6%), while conversely conduct disorders were significantly higher (80%) in those from broken homes than in those from intact homes (44.2%). Of the 12 children from intact homes who had experienced prolonged separation, 11 (92%) showed conduct disorders, compared with 39% of those who had not suffered separation. In contrast the incidence of neurotic disorders among those who had been separated was only 17%, compared with 50% in those who had not; further, 8 (66%) of these separated children were educationally retarded, compared with 35% who had not been separated. In the children from broken homes there was no marked difference in behavioural abnormalities between those who remained with their mothers and those who did not, the incidence of conduct disorders being respectively 88 and 74%, and of neurotic symptoms 31 and 15% respectively.

In a further study of the possible relationship between an adverse childhood environment of the parent or parents and the present disturbance of the child, only those children from intact homes who had not experienced separation were investigated. When both parents had had intact homes in childhood only 24% of the children suffered from conduct disorders, while 68% showed neurotic symptoms; in contrast, when at least one parent had had a broken home in childhood 52% of the children suffered conduct disorders and only 34% neurotic disorders. There was no significant difference in the proportions of behavioural abnormalities in the children when it was the mother, or the father, or both parents who suffered a broken home in childhood, though it is admitted that the numbers of children in these subgroups were small. The evidence derived from this study is discussed at some length and various suggestions for future treatment are made.

[Interesting as this paper is, it should be noted that the author himself states that "since no comparable figures are available for the general population it cannot be asserted certainly that these findings differ from those which would be found for a normal population of school children".]

David Morris

189. The Evaluation of the Clinical Significance of Antibodies to Brain in the Serum of Schizophrenics and Patients with Other Neuropsychiatric Illnesses. (К оценке клинического вначения противомозговых антител в сыворотке больных шивофренией и другими нервно-психическими заболеваниями)

S. F. SEMENOV, G. B. MOROZOV, and N. I. KUZNECOVA. Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1210–1215, No. 8, 1961. 19 refs.

In this paper from the Institute of Forensic Psychiatry, Moscow, the authors refer briefly to a previous paper from the same source concerning 127 patients suffering from various neuropsychiatric, disorders, in 33 of whom antibody to brain was discovered in the serum (Kuznecova and Semenov, Z. Nevropat. Psihiat., 1961, 61, 869). They now present a clinical analysis of these patients.

Of 84 patients with schizophrenia, 22 had circulating brain antibody in titres ranging from 1:40 to 1:80. In 8 of these 22 cases there were various varieties of remission, but the remainder showed active symptoms. Their ages ranged from 9 to 55. The majority suffered from paranoid schizophrenia, although there were also hypochondriacal, catatonic, and simple varieties. The duration of illness ranged from less than a year to 11 years and more. Although half the patients had complications such as alcoholism, pulmonary tuberculosis, and bronchial asthma, the other half were free from complications. Thus it was felt that the presence of antibodies must be attributed to the basic schizophrenic disease process. In many cases there was no parallel between the clinical state and the blood content of antibody. The presence of antibody in several cases of schizophrenic end-state leads the authors to regard these as being states of latent activity rather than completed processes.

Circulating brain antibody was also found in 11 nonschizophrenic patients, mostly with organic brain disease. This group included 5 out of 13 cases of post-traumatic state, 2 out of 3 of neurosyphilis, one case of postencephalitic character disorder, one of chronic alcoholism with somatic neurological and psychic disturbances, and 2 of " reactive state", one with hysterical neurological symptoms and the other paranoid, both leading to permanent personality change. Eighteen out of the 22 schizophrenics showed eosinophilia, monocytosis, and an increase in the percentage of staff forms in the blood, unaccompanied in most of them by physical illness or increased erythrocyte sedimentation rate. Nine of the remaining 11 patients showed eosinophilia, monocytosis, leucocytosis, and a raised erythrocyte sedimentation rate.

The authors consider that whether the observed antibody reflects a defence mechanism or represents a true autoneurotoxin is a matter for future research.

G. P. McGovern

190. The Suicidal Fit: a Psychobiologic Study on Puerto Rican Immigrants

E. C. TRAUTMAN. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 76-83, July, 1961. 12 refs.

At the Lincoln Hospital, New York, the author undertook a psychiatric exploration of a special group of people who had survived a suicidal attempt, namely, 93 Puerto Rican immigrants, 17 male and 76 female. He shows how all the suicide attempts were made during the height of emotional excitement in the same way and in similar circumstances, and calls the composite picture "the suicidal fit". In all cases the act was sudden, impulsive, and precipitated by some extreme emotion such as anger, despair, or anxiety. There were two phases, first retreat from the stressful scene to privacy. and then the swallowing of such poison as was at hand in the form of barbiturate, domestic cleanser, or other chemical. All the patients claimed inability to withdraw from the situation, despite mounting tension, until a state of loss of control was reached. In this frame of mind the subject took the poison without fear of death, desiring only peace and relief. At this moment death presented as a very limited concept. The author doubts whether this reaction should be regarded as a true suicidal action. There may be a basic suicidal state, however, which is triggered off by some final factor, such as an insult or unfriendly letter.

Among the women, 43 attempts resulted from a quarrel with husband or lover and 14 from a quarrel between mother and daughter, while 12 were depressed for various reasons. Of the men, 11 had quarrelled with wife, girl-friend, or a parent, 2 had lost their jobs, and one was evicted for non-payment of rent. The women showed greatly increased tendency to impulsive suicide attempts during menstruation. The age range was 12 to 47 years, with the peak incidence in women at 18 to 20 and in men between 27 and 29. Once the poison had been taken a reaction set in, the fear of death returned. and the subject developed extreme dread of the possibly fatal consequences. In many cases this was followed by a remarkable swing to optimism, the subjects expressing a determination to change their lives. Family and friends were also affected by this state of affairs. [The result of these emotional swings of mood is not stated, as there was apparently no follow-up study]. However, the author makes the point that the important feature was a combination of the impulse to escape from a situation, with temporary breakdown of the normal resistance to death._ Gavin Thurston -

191. "Functional" Disorders: a Follow-up Study of Out-patient Diagnosis

H. JACOBS and W. RITCHIE RUSSELL. British Medical Journal [Brit. med. J.] 2, 346-349, Aug. 5, 1961. 6 refs.

At general hospitals a large proportion of out-patients present with disorders that are psychogenic rather than organic in origin. Responsibility for making a differen-

tial diagnosis lies with the consultant; in the opinion of the authors of this paper from the United Oxford Hospitals he is also, with his knowledge of relevant organic disease, in the best position "to correct unreasonable fears and adjust problems of living which are having a harmful effect". The follow-up study they describe was designed to ascertain whether the initial opinion as to absence of organic disease was correct and, on the assumption that usually "simple and authoritative reassurance is what is chiefly needed", to what extent this advice was effective.

Approximately 2,000 new out-patients were seen by two consultants in one Oxford neurological out-patient clinic in 1954 and 1955. From these, 100 patients were selected whose case records indicated that they had no significant organic disease; they had received little clinic treatment other than reassurance and advice. The majority were followed up 5 years later, attention being directed towards the presence of organic disease. Six patients could not be traced; of the remaining 94, 80 were in good health, though in 26 some minor symptoms persisted. Details are given of the 14 patients who had developed some organic disorder, which in 5 instances was probably related to their original presenting complaints.

While stressing the need to reduce even this error, the results show a more accurate differentiation between organic and functional disorders than has been reported previously. As regards the benefit of the advice to the patient's mental health, the authors state that there are no means of determining this accurately, but the generally good prognosis in these cases; based on the reports of the patient's own doctor, accords with the findings of other workers.

Alan A. Black

PSYCHOSOMATIC MEDICINE

192. Psychosomatic Medicine and the Behavioral Sciences

J. Ruesch. Psychosometric Medicine [Psychosom. Med.] 23, 277-286, July-Aug., 1961. Bibliography.

Current concepts in psychosomatic medicine are critically reviewed in this paper from the University of California School of Medicine, and the Langley Porter Neuropsychiatric Institute, San Francisco. The limitations of dichotomous models-for example, "mindbody" and "man-environment"-are discussed, and the present need for a unifying theory is emphasized. Psychosomatic medicine is broadly viewed as a field of study in which physical disease is appraised in the light of the patient's behaviour. Some problems arising from the multi-disciplinary team approach in research are discussed, an important one being semantic difficulties in communication. There are few established facts in psychosomatic medicine, and these are mainly concerned with "transactional" rather than causal relationships. Sociocultural studies may add a significant dimension to psychosomatic research. In the last analysis, however, research activity requires to be directed towards learning more about the mediating mechanisms which transform

inner experience into bodily pathology. Limited, well-controlled investigations, rather than diffuse studies, are necessary for future advances.

A. Balfour Sclare

193. Ecological Observations of the Relation of Physical Illness, Mental Illness, and the Social Environment
L. E. Hinkie. Psychosomatic Medicine [Psychosom. Med.] 23, 289-296, July-Aug., 1961. 1 fig., 10 refs.

In this paper from the New York Hospital-Cornell Medical Center, a review is presented of research work on the relationship between environmental stress and patterns of illness. The contribution of the social psychiatrist to this type of ecological study is discussed. The occurrence of illness patterns is considered in association with such environmental factors as social class, social mobility, change in status, economic conditions, migration, and acculturation. The social psychiatrist in this mode of research investigation makes an appraisal of "the probable meaning of the stressful situation to the individual". This is achieved by assessing a number of environmental variables as well as each subject's past and present circumstances. These "non-medical" data are then correlated with the medical data concerning patterns of illness.

Ecological surveys thus require to take account of both the "outer" and "inner" worlds of the individual. The results of a series of investigations carried out in recent years by the author and his colleagues lend little support to the widely held view that there exists a specific group of "psychosomatic" disorders. Rather, they suggest that threatening or challenging environmental situations are non-specifically correlated with a high occurrence rate of illness, both physical and mental, in certain vulnerable individuals.

A. Balfour Sclare

194. Hostility in Verbal Productions and Hypnotic Dreams of Hypertensive Patients: Studies of Groups and Individuals

S. M. KAPLAN, L. A. GOTISCHALK, E. B. MAGLIOCCO, D. D. ROHOVIT, and W. D. ROSS. *Psychosomatic Medicine* [*Psychosom. Med.*] 23, 311-322, July-Aug., 1961. 20 refs.

The quantitative aspects of hostile aggressive impulses in patients suffering from essential hypertension were studied at the Cincinnati General Hospital, Ohio, a group of 10 hypertensive patients being matched for age and sex with a group of 10 non-hypertensive subjects. In addition 2 hypertensive subjects were studied more extensively. The method of "verbal sampling" was used—that is, each subject was asked to speak freely for 5 minutes about any dramatic or personal experience he had had or was having. One hypertensive subject was hypnotized on several occasions and dreams occurring during the hypnotic sessions were noted. Blood pressure was recorded before, during, and after both the verbal samples and the hypnotic trances. The hostile aggressive content of the verbal samples and the hypnotic dreams was rated by means of a modification of the method of Saul and Sheppard (J. Amer. psychoanal. Ass., 1956; 4, 486) and also by means of Gottschalk's technique (A.M.A. Arch. Neurol. Psychiat., 1958, 79, 688).

A positive correlation was found between blood pressure levels and the values for hostile content in the hypertensive subjects, but not in the normotensives. It is pointed out that care must be taken in interpreting this finding since the results are not sufficiently far-reaching to indicate the nature or actiology of essential hypertension. The hostility level may produce a raised blood pressure level or vice versa, or both may be related to an unknown common factor.

[Although the experimental and control groups were said to be matched for race, it is elsewhere stated that the experimental group consisted entirely of negroes while the control group contained 7 negroes and 3 white subjects.]

A. Balfour Sclare

AFFECTIVE DISORDERS

195. Depression and Childhood Bereavement

F. Brown. Journal of Mental Science [J. ment. Sci.] 107, 754-777, July [received Sept.], 1961. 5 figs., 21 refs.

The incidence of loss of parents during childhood has been investigated in 216 unselected patients suffering from depressive illness attending the Hampstead General Hospital Psychiatric Department. Control figures were taken from the 1921 orphanhood tables from the 1921 census. A second series of controls were taken from 267 patients attending Hampstead general practice surgeries. The incidence of childhood bereavement was significantly higher in the depressive patients than in both the general population and Hampstead general practice patients. For instance 41% of depressive patients lost either parent before the age of 15, compared with 12% from the Census, and 19.6% from Hampstead general practice. The loss of fathers was more significant in later childhood in the age groups 5 to 9 and 10 to 14. The loss of mothers was equally significant in each five-year period of childhood. From this it is concluded that bereave-" ment in childhood is one of the most significant factors in the development of depressive illness in later life. There was a significantly higher proportion of depressive patients who had no knowledge of their parents than in the general population. The theory is put forward that depression in later life often occurs through the re-activation by possibly minor rejection situations of an apparently recovered depression in childhood. The therapeutic and prophylactic implications of this theory are discussed.—[Author's summary.]

196. Memory Functions in Endogenous Depression Before and After Electroconvulsive Therapy

B. Cronholm and J. O. Ottosson. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 193-199, Aug., 1961. 14 refs.

From Karolinska Institutet, Stockholm, the authors report the results of three investigations of memory functions in depressed patients before and after electric convulsion therapy (E.C.T.). Three memory tests were used, each in two equivalent forms. The immediate recall of presented data (regarded as indicating learning ability) and their delayed recall after 3 hours (regarded

as indicating both learning ability and memory retention) were scored. The patients had not previously had E.C.T. for at least 6 months, if ever.

In the first investigation the memory functions of 20 mildly depressed and 20 non-depressed surgical patients (matched for sex, age, intelligence, education, and rural or urban residence) were tested. Both immediate and delayed recall was significantly worse in the depressed patients. The difference between immediate and delayed recall (regarded as indicating memory retention) was the same in both types of patient. From this it is concluded that in depressed patients learning ability is reduced, but the retention of learned material normal.

The second investigation concerned the influence of E.C.T. (2 or 3 times weekly) on the memory performance of 42 patients whose endogenous depression had improved after treatment. Memory tests were given one or two days before the first E.C.T. and one week after the fourth. It was found that there was a significant improvement in immediate recall after treatment, but no change in delayed recall. The conclusion was drawn that learning ability had improved, but retention had deteriorated.

The third investigation examined the relationship between improved clinical state after E.C.T. and changes of memory functions in 45 patients, of whom only 3 were unimproved. Three modifications of E.C.T. had been applied which yielded different degrees of clinical improvement. With the most successful modification there was also the greatest improvement in both immediate and delayed recall, whereas with the least successful modification immediate recall was slightly improved and delayed recall worse. However, a closer study of the relation between memory improvement and clinical improvement yielded regression coefficients which were not significant. In spite of this negative result, the authors conclude that clinical improvement is related to increased learning ability, whereas the impaired memory retention "-may be regarded as a direct, adverse effect of E.C.T.". F. K. Taylor

SCHIZOPHRENIA

197. Disorders of Attention and Perception in Early Schizophrenia

A. McGHIE and J. CHAPMAN. British Journal of Medical Psychology [Brit. J. med. Psychol.] 34, 103-116, 1961.

Observations derived from an earlier study of schizophrenia (Freeman et al., Chronic Schizophrenia, London, 1958) suggest that the basic psychopathology of schizophrenia consists in impairment of ego functions, principally in the process of perception. The basic disorder in schizophrenia may thus be regarded as a cognitive disturbance causing the patient to operate at a relatively primitive and unorganized perceptual level. Other aspects of the symptomatology may then be interpreted as reactions to this disorder.

The present communication from Dundee Royal Mental Hospital reports the outcome of studies on 26 early schizophrenic patients; the diagnosis was confirmed in

each case by the subsequent course of the illness. Patients were interviewed informally for periods varying from 2 to 12 hours and verbatim notes were made. A full range of topics was discussed in standardized form to focus on abnormalities in (1) attention, (2) perception, (3) motility, (4) thinking, and (5) affect. The interview material was analysed, being broken up into a number of separate statements each representing the patient's description of a subjective alteration in experience. The separate statements were arranged by the authors in categories according to the main areas of cognitive function, as enumerated above. Disturbances in attention seemed to be characterized by loss of ability to direct attention focally; it followed from this that the patient reported feelings that his personal identity was threatened by a flood of incoming impressions. Disorders of perception included: changes in sensory quality, in particular heightening of sensory vividness; altered perception of speech, in which details of form became unduly prominent and masked appreciation of content: and abnormal interactions between perception and movement. movement being hindered by the confused perceptions. These disorders may all be described as deriving from a conscious awareness of perceptual features which normally function autonomously. Disorders of motility were described principally as disintegration of movement occasioned by an obtrusion into awareness of the components of motor responses, that is, as a need for conscious coordination of any simple sequence of movements. The patients thus described loss of spontaneity associated with a heightened awareness of sensations and volitional impulses normally outside conscious experience. Changes in the process of thinking were characterized by disorders of control, direction, selection, and inhibition of thought content. Affective changes. reported consisted in perplexity and acute anxiety accompanied by a certain amount of insight, later followed by experience of loss of subjectivity. The authors suggest that these affective changes are secondary to the patient's awareness of the primary cognitive changes.

The authors discuss their findings and claim that they support the hypothesis that a primary disorder in schizophrenic illness takes the form of a decrease in the selective and inhibitory functions of attention, which leads in turn to a number of other pathological changes.

R. H. Cawley

198. The Non-Psychotic Residue in Schizophrenia J. M. Davie and T. Freeman. British Journal of Medical Psychology [Brit. J. med. Psychol.] 34, 117-127, 1961. 8 refs.

The authors, writing from Glasgow Royal Mental Hospital, discuss the concept of the non-psychotic residue in schizophrenia, which they define as that area of normal mental functioning which becomes apparent from time to time, indicating that certain mental processes have not been affected by the disease. In the conceptual framework of psychoanalysis the non-psychotic residue may be identified with those ego functions which have escaped involvement in the psychotic disturbance.

Disturbances of cognitive processes are of common occurrence in schizophrenia, and the authors provide

clinical illustrations to demonstrate the manner in which directed verbal communication reflects the degree of integrity of conceptual thought and the capacity for perceiving such thoughts. The transition, which may be rapid, from well-ordered to nonsensical and irrelevant verbal communication demonstrates the existence of fluctuations in the level of such functions. These fluctuations seem to be determined by changes in the psychic economy similar to those described by Freud in his account of the primary and secondary processes. Fluctuations in constancy and stability of visual percepts may also occur. It is emphasized that the concept of "nonpsychotic" has no particular topographical significance; it is rather a description of a means whereby mental processes emerge from a state of dedifferentiation as a result of some alteration in psychic economy.

The authors quote various examples of expression of castration anxiety, homosexual conflict, and other features of the thought content of schizophrenic patients and suggest that the role of unconscious conflict is of paramount importance in the formation of schizophrenic symptoms—that is, such non-psychotic conflicts may colour or modify-the psychotic symptoms and may determine their content. They state that unconscious conflicts of this type may precipitate a schizophrenic state as well as providing the ideational material whereby the psychotic process finds some form of mental representation. They emphasize, however, that these conflicts are not specific to schizophrenia and must be distinguished from the so-called primary psychotic mechanisms.

The implications in transference manifestations are discussed; it is suggested that the frequency of non-psychotic transference manifestations will be dependent upon the extent to which the ego functions remain intact and upon the degree to which the libido can still effect object cathexis. Transference phenomena may be non-psychotic, even in chronic schizophrenics, whereas progressive damage to the synthetic functions of the ego and to the capacity for object cathexis is associated with concurrent diminution of non-psychotic transference phenomena.

It is suggested that it is of value to draw a sharp distinction between the psychotic and non-psychotic processes in the understanding and treatment of schizophrenic patients. The psychotic process consists of a dedifferentiating sequence which may affect all the functions of the ego and impair the capacity for object cathexis. Prominent among the non-psychotic processes are the unconscious conflicts which supposedly play some part in initiating the illness and which are represented to some extent in the content of the symptoms.

R. H. Cawley

199. Admitting Schizophrenic Mothers with Their Babies A. A. Baker, M. Morison, J. A. Game, and J. G. Thorpe. Lancet [Lancet] 2, 237-239, July 29, 1961. 5 refs.

In 1959 a special unit was set up at Banstead Hospital, Sutton, Surrey, to which schizophrenic mothers were admitted together with their babies. In this paper the results in the first 20 patients treated in the unit are compared with those in 20 similar patients treated earlier. by the same physician in an admission ward without their babies; all the patients were diagnosed as suffering from puerperal schizophrenia. On admission the average rating on the Wittenborn Scale for severity of illness was greater for the patients treated in the unit (34.6) than for the earlier group (29.4), but on discharge it was less (13.6 and 17.6 respectively). Also the average duration of stay in the unit was shorter (10 weeks compared with 16 weeks). All 20 patients treated in the unit were discharged home in "social remission" and able to care for their baby, compared with only 13 of the comparative group; further, the relapse rate within 6 months of discharge was much greater in the latter group (10 cases compared with 3). The most successful treatment proved to be up to 20 treatments with electric convulsion therapy, followed by chlorpromazine, both being found to be necessary for a well maintained social remission. The mother was encouraged to breast-feed her baby and to look after it herself as much as possible. Overt hostility or hate for the baby proved rare, though without the help of the nursery staff neglect might have occurred.

It is concluded that schizophrenic patients can be excellent mothers and feel deeply for their babies and that to have the baby with them is therapeutically beneficial. It is also, of course, beneficial for the healthy emotional development of the infant, who would otherwise suffer deleterious separation from his mother at a crucial time.

[Although this study was uncontrolled and no statistical analysis of the results is attempted, it is nevertheless invaluable as a description of a successful experiment worth repeating elsewhere.]

Christopher Wardle

200. The Subtypes of Schizophrenia in the Light of Long-term Observations. (Die Typologie schizophrener Psychosen im Lichte der Verlaufsbetrachtung)
W. Janzarik. Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.] 202, 140–154, 1961. 28 refs.

Kraepelin's division of schizophrenia into the subtypes of hebephrenia, paranoid, and catatonia was tested by investigating the morbid history of 100 chronic schizophrenic in-patients in a mental hospital, the object being to discover whether the types had on the whole remained constant throughout the illness or whether most of them had changed from one type to another. The histories of the 50 men and 50 women studied extended over at least 20 years, and the average duration of the illness 35 years, of which an average of 25 years was spent in hospital.

Almost all the patients had passed at one time or another through a period of the paranoid-hallucinatory type, the only exception to this being a group of catatonic patients. In general, change of type predominated over constancy of type. The author concludes that the clinical picture is the product of a number of factors and their interaction, namely, acute psychotic attacks, lasting defects in the sphere of affect and drive, and a fundamental reorientation in the patient's outlook. Whichever of these three factors predominates will determine the clini-

cal character of the psychotic period. The three factors correspond respectively to the catatonic-impulsive periods, the flat and featureless personality changes, and the delusional states, with many transitional forms.

J. Hoenig

201. Urinary Aminochromes in Schizophrenia: Chromatography of Lead-acetate-extractable Chromogens R. L. Veech, L. B. Bigelow, W. D. Denckla, and M. D. Altschule. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 127–130, Aug., 1961. 4 refs.

In this study reported from McLean Hospital, Waverley, Massachusetts, the authors sought to extend their earlier observations suggesting that urine from schizophrenic subjects contains substances (referred 'to as aminochromes) chemically related to adrenolutin and adrenochrome. The subjects (19 schizophrenic patients and 20 normal controls) ate the same diet. [Evidence of stricter dietary control is not presented.] Urine samples (aliquots of 12-hour collections) were adjusted for specific gravity differences and treated in the presence of various reducing substances with lead acetate. The resulting precipitate was separated, decomposed with hydrogen sulphide, and the soluble products examined by paper chromatography. Two or more control urine samples to which adrenolutin, adrenochrome, or adrenaline (1mg. of each) was added before analysis, control samples with no additions, and samples from patients were carried through the procedure in parallel. Of the samples from patients, 14 showed a yellow fluorescent spot on chromatography. A similar spot in the same position was observed in all the control samples to which adrenolutin or adrenochrome (but not adrenaline) had been added, but in only 2 of the control samples with no additions. Various solvent systems and chemical tests were applied to the material from the patients in an endeavour to confirm its origin from adrenolutin or adrenochrome, but with inconclusive results. R. Rodnight

202. A Comparison of Tetrabenazine and Chlorpromazine in Chronic Schizophrenia

G. W. ASHCROFT, E. J. MACDOUGALL, and P. A. BARKER. Journal of Mental Science [J. ment. Sci.] 107, 287-293, March [received Aug.], 1961. 5 refs.

Tetrabenazine (TBZ), a benzoquinolizine derivative, is a new 'drug which' has shown promising experimental and clinical effects resembling those of reserpine, except that depression of the concentrations of 5-hydroxytryptamine and catecholamines in the brain lasts only 24 hours, compared with 6 to 7 days in reserpine-treated animals. Also the drug does not produce such side-effects as bradycardia and hypotension, which often occur with reserpine.

The present controlled trial was carried out at the Royal Edinburgh Hospital in order to compare TBZ with chlorpromazine in the treatment of chronic schizophrenia and to determine the range of usefulness and side-effects of the new drug. The subjects were 52 female chronic schizophrenic patients, who were divided into two equally matched groups. During the initial 6 weeks of the study all day medication was stopped; if night sedation was required 200 mg. of amylobarbitone sodium

was given: During the 7th and 8th weeks all the patients received one placebo capsule three times a day. From the 9th to 20th weeks patients in one group were given, under double-blind conditions, TBZ in a dosage of 30 mg. 3 times a day for 4 weeks and then 40 mg. 3 times a day for the remaining 8 weeks, the other group similarly receiving 75 and then 100 mg. of chlorpromazine 3 times a day. Patients were assessed by detailed examination carried out by the same physician first during the placebo period and again during the 20th week. From the beginning of the 6th week onwards patients were also assessed daily by the nurse-in-charge on 10 items on the Baker and Thorpe behaviour rating scales, which measure schizophrenic deterioration and restlessness.

Results among the 44 patients (20 and 24 respectively) who completed the trial showed that behaviour ratings in both groups improved significantly, restlessness being improved more by chlorpromazine and thought disorder by TBZ. Side-effects were more troublesome in the TBZ-treated group, and details are given of the 5 patients who had to be withdrawn from the trial, 2 because they developed subacute delirium, one generalized tremor, one marked unreality feelings and agitation, and one who became suicidally depressed. Less severe sideeffects included catatonic stupor (one case), Parkinsonism (1), drowsiness (2), and restlessness (4). None of the cardiovascular complications seen with reservine therapy occurred and, apart from depression, all side-effects subsided within 24 hours of discontinuing treatment. The authors consider that TBZ may be useful in the treatment of phenothiazine-resistant chronic schizophrenic patients and that it is worthy of more extensive Alan A. Black

203. The Etiology of Schizophrenia: a Review
A. J. FERREIRA. California Medicine [Calif. Med.] 94, 369-377, June, 1961. Bibliography.

TREATMENT

204. Therapeutic Value of Thioproperazine and the Importance of the Associated Neurological Disturbances J. DENHAM and D. J. E. L. CARRICK. *Journal of Mental Science [J. ment. Sci.]* 107, 326-345, March [received Aug.], 1961. 35 refs.

At Long Grove Hospital, Epsom, 58 deteriorated schizophrenic patients (16 women and 42 men) who had been ill for an average of 10 years were treated with thioproperazine over a period of 11 months. Chronicity and resistance to previous treatment made the group largely self-controlled. After all other forms of medication had been stopped for 4 weeks 51 of the patients were given discontinuous treatment, starting with 5 mg. of thioproperazine three times a day and increasing daily until maximum muscle hypertonia was induced, when the dose was kept at that level for 5 days and then interrupted. After a few days muscle tone returned to normal and maximum psychiatric improvement could be observed: when this was incomplete further modified courses were given; when adequate a maintenance dose

of 1 to 10 mg. daily was started; on the average, three courses were required. The other 7 patients received continuous treatment with slowly increasing doses over several weeks.

Total symptomatic remission was obtained in 32 of the 58 patients, while 10 were considered to be much improved and 15 improved. The appearance of early, even if initially transient, mental improvement, of florid symptoms in apathetic patients, and of swings of mood was indicative of a favourable prognosis, as was also the development of widespread muscular hypertonia.

A wide variety of neurological changes occurred. These resembled those of epidemic encephalitis and tended to fall into similar, and broadly chronological. patterns of akinetic, akineto-hypertonic, and hyperkineto-hypertonic states. (Because of marked individual variation the neurological phenomena are described in detail.) Concomitant autonomic disturbances were also seen, chiefly excessive production of sweat, sebum, and saliva. Excitomotor attacks occurred in 8 patients during the first few days of treatment and were similar to those seen with other phenothiazines. The authors comment on the contagious nature of these attacks; they also emphasize the heightened suggestibility which was noted from the earliest days of treatment and which often facilitated later psychotherapy. Successful treatment with thioproperazine was correlated with the degree and extent of muscular hypertonia. Moreover, if the latter did not occur or was suppressed with anti-Parkinsonian drugs, improvement did not usually occur during that particular course of treatment; excitomotor attacks were therefore best treated with paraldehyde. All secondary neurological effects disappeared within a few days of stopping treatment and relatively few other complications occurred.

Following up the analogy drawn between the thioproparazine-induced neurological disturbances and those described in epidemic encephalitis, the authors discuss the relevant neurophysiological concepts and postulate that both drug and virus have a similar site of action, namely, the reticular formation of the brain stem.

Alan A. Black

205. The Comparative Effectiveness of Six Phenothiazine Compounds, Phenobarbital and Inert Placebo in the Treatment of Acutely III Patients: Global Measures of Severity of Illness

A. A. Kurland, T. E. Hanlon, M. H. Tatom, K. Y. Ota, and A. M. Simopoulos. *Journal of Nervous and Mental Disease [J. nerv. ment. Dis.*] 133, 1–18, July [received Oct.], 1961. 23 refs.

Four years ago a project was initiated at Spring Grove State Hospital, Baltimore, to study the relative effectiveness of the phenothiazine compounds promazine, chlorpromazine, mepazine (pecazine), triflupromazine (fluopromazine), prochlorperazine, and perphenazine in the short-term treatment of acutely ill patients. This, one of a series of papers, is concerned with the differential effects of these drugs on two "global" measures of severity of illness: the Multidimensional Scale for Rating Psychiatric Patients (M.S.R.P.P.), completed every 2 weeks by a clinician and a ward observer and used to measure total

morbidity; and a psychiatric rating on adaptability, made weekly. Newly admitted patients, selected to meet symptomatic criteria and mostly schizophrenic, were allocated at random to treatment on a double-blind basis with one of the phenothiazines or phenobarbitone or an inactive placebo. After a 48-hour drug-free period medication was given parenterally for 48 hours and then orally for the remainder of the 6-week study period. Apart from a specified minimum daily level, dosage was left to the discretion of the physician, who was also free to withdraw patients whose response to treatment was unsatisfactory. The total number of patients studied was 238.

Mean M.S.R.P.P. and adaptability scores for each treatment, adjusted to control for initial severity of illness. were compared with the means for every other drug group after 2 weeks and at the end of treatment. On the basis of total M.S.R.P.P. morbidity change perphenazine, prochlorperazine, triflupromazine, and chlorpromazine were therapeutically more effective than mepazine, promazine, or the placebos. With the exception of perphenazine, the grouping on the basis of the adaptability rating was similar. For all comparisons triffupromazine was most consistently the best drug, followed closely by chlorpromazine. Attrition effects, partly due to the design of the experiment, were considerable. Altogether 81 patients were withdrawn from the study because of lack of improvement, thus distorting the failure sample; however, as there was a rank order correlation of -0.96 between the number of patients withdrawn from each drug category and the previously estimated potency of the drug (in terms of its recommended minimum dosage), the procedure of withdrawing "failures" from the patient sample favoured the least potent drugs. A further 25 patients were removed from the trial because of somatic reactions. Perphenazine accounted for 8 and triflupromazine for 4 of the 14 cases of neurological complications. Among the 11 other somatic disturbances, vasomotor episodes occurred 6 times.

The results are compared with those of other similar studies. There is general agreement about the relative efficacy of the drugs and also about the observation that if patients are going to improve at all, they do so after 2 weeks of treatment. Patients given perphenazine were an exception. The point is again raised that potency may be related to the appearance of neurological complications, but these may either mask improvement or result in the premature withdrawal of treatment from the patient.

A discussion of the ratings and the statistical model used in this study touches on some of the more general problems of drug evaluation.

Alan A. Black

206. Psychopathological Experiences after Uni- and Bilateral Psychosurgical Operations. (Psychopathologische Erfahrungen bei ein- und beidseitigen psychochirurgischen Eingriffen.) [Review Article]

W. Deinen. Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgeblete [Fortschr. Neurol. Psychiat.] 29, 353-422, July, 1961. 1 fig., bibliography.

Paediatrics

207. A Follow-up Study of Hyperbilirubinaemia in Fullterm Infants without Iso-immunisation. [In English] J. Bjure, G. Liden, T. Reinand, and A. Vestby. Acta paediatrica [Acta paediat. (Uppsala)] 50, 437-443, Sept., -1961. 15 refs.

In 113 full-term infants born in two maternity hospitals in Gothenburg in 1956 and 1957, none of whom showed evidence of haemolytic disease of the newborn. the serum bilirubin level exceeded 18 mg. per 100 ml. An exchange transfusion was carried out on 32 of these infants, but there were also 30 in whom the bilirubin level exceeded 22 mg. per 100 ml. but who did not receive a transfusion. No signs of kernicterus were observed. In the present paper the results are reported of a followup examination of these infants when they were aged 2 to 3 years. None of the children showed deafness of the central type. The I.Q. distribution (as determined by the responses to Merrill-Palmer tests) among the jaundiced infants was similar to that in a control group of 51 infants showing minimal jaundice. Evidence of brain damage was found in 3 infants, and in each case it could be explained on the basis of complications occurring during delivery.

It is concluded that in full-term infants exchange transfusion is not required for hyperbilirubinaemia in the absence of haemolytic disease unless there are other circumstances which might impair the blood-brain barrier or facilitate liberation of bilirubin from the bilirubin-albumin complex.

F. P. Hudson

208. Gamma Globulin against Rubella in Pregnancy.

I. Prevention of Maternal Rubella by Gamma Globulin and Convalescent Gamma Globulin: a Follow-up Study.

[In English]

R. LUNDSTRÖM, C. THORÉN, and B. BLOMQUIST. Acta paediatrica [Acta paediat. (Uppsala)] 50, 444-452, Sept., 1961. '27 refs.

In the present investigation, 251 women—who in 1956 had been exposed to rubella in the first 4 months of pregnancy—were given 4 ml. of convalescent gamma globulin. An account is given of a follow-up study, with examination of their children at 2 to 3 years of age. All but 5 cases were traced. Despite treatment, 6 women contracted rubella—an attack rate of 2.4%. Three of these 6 women aborted, and one had a child with malformations of the rubella syndrome type. Two of the 245 women showing no signs of manifest rubella had children with defects that might be ascribed to inapparent maternal rubella. Another 28 pregnant women were given 24 ml. of ordinary pooled gamma globulin. None contracted rubella, 2 had spontaneous abortions, and one gave birth to a child with mongolism.

The present investigation indicates that convalescent gamma globulin and ordinary gamma globulin have a protective effect against rubella. The following dosage is recommended for future use in pregnant women exposed to rubella. Rubella convalescent gamma globulin (12%), 12 ml. i.m. as soon as possible after exposure; when this is not available, pooled gamma globulin (12%), 24 ml. i.m.—[Authors' summary.]

209. Gamma Globulin against Rubella in Pregnancy. II. Manifest Maternal Rubella in Early Pregnancy Treated with Convalescent Gamma Globulin: a Follow-up Study. [In English]

R. LUNDSTRÖM, C. THORÉN, and B. BLOMQUIST. Acta paediatrica [Acta paediat. (Uppsala)] 50, 453-456, Sept., 1961. 13 refs.

Rubella convalescent gamma globulin was given to 28 women with rubella in early pregnancy. Of those treated in the first trimester, pregnancy terminated in foetal death in 32% and 11 of 21 offspring survived. At the age of 3 to 4 years, 4 of the 21 survivors showed abnormalities belonging to the rubella syndrome. Administration of antibodies to women with manifest rubella in early pregnancy did not succeed in preventing foetal damage.—[Authors' summary.]

210. Causes of Death in Infants with Hemolytic Disease of the Newborn (Erythroblastosis Fetalis)
R. VAN PRAAGH. *Pediatrics* [*Pediatrics*] 28, 223-233, Aug., 1961. 27 refs.

This paper analyses the causes of death in 74 out of 882 live-born infants with haemolytic disease admitted to the Children's Hospital Medical Center, Boston, during the 7 years ending in December, 1956. The total number of deaths was 82, but complete necropsy was performed on only 74. As 70 of these babies died within 7 days of birth an unselected group of 70 infants without haemolytic disease who died at 7 days of age or less during 1955-6 and who also came to necropsy were used for some "control" comparisons.

Of the 74 infants on whom necropsy was performed, death was associated with severe haemolytic disease in 44, delay in treatment in 15, and conditions not related to haemolytic disease in 15. In the 44 with severe haemolytic disease the average haemoglobin concentration was 7.5 g. per 100 ml., heart failure was present in 35, and 27 had evidence of aspiration of amniotic fluid. Pulmonary haemorrhage was noted in 23 cases, but the incidence and severity of this finding was similar in the "control" group. A ruptured spleen was found in 4 infants; all were extremely anaemic and flaccid and distension of the abdomen hampered palpation, but in the 3 who survived long enough for the introduction of a catheter into the umbilical vein a very low venous pressure was found, in contrast to the raised pressure usually present in babies with very severe haemolytic disease. Intraventricular cerebral haemorrhage was seen in 3 cases; all were mature infants and died within 7 hours

with evidence of widespread petechial haemorrhage. Of the total number of 882 infants, 31 developed kernicterus, but only 6 were admitted to hospital during the first 24 hours of life, the majority being first seen on the 3rd or 4th day; 13 of the 31 died, only 2 being premature. Haemorrhagic features were not prominent at necropsy apart from pulmonary haemorrhage, which was found in 9 cases, while 2 infants died from severe late anaemia.

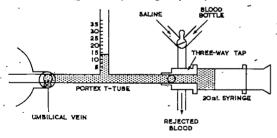
Death occurred during or shortly after exchange transfusion in 25 infants, on 24 of whom necropsy was performed. In 9 the marked severity of the haemolytic disease and its complications were sufficient to account for death. In 13 infants, of whom 5 were premature, death was due to cardiac arrhythmia; in 7 of these no significant pathological lesion was found at necropsy, but 4 showed evidence of considerable aspiration of amniotic fluid, in some cases associated with pneumonia, while 2 of the 13 infants collapsed during the administration of calcium gluconate. In only 2 infants in the whole series was death associated with excessive trauma due to technical difficulty in performing the exchange transfusion, though the procedure was often carried out by "relatively inexperienced members of the house staff".

No biochemical data are given, but the author discusses the possible role of metabolic acidosis in causation of death, particularly in premature infants and those with heart failure or pulmonary complications, and he suggests that the use of heparinized blood might reduce this danger. The importance of pulmonary haemorrhage is also considered and further study of this problem is urged.

F. P. Hudson

211: A New Technique in Exchange Transfusion T. WRIGHT. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 400-403, Aug., 1961. 1 fig., 6 refs.

Exchange transfusion was performed on 15 occasions on 10 babies suffering from haemolytic disease at St. George's Hospital, Lincoln, the venous pressure being recorded frequently. The indications for and technique of exchange transfusion were those generally adopted, except that the "portex" umbilical catheter attached to the transfusion apparatus had a side-piece for recording the venous pressure (see diagram). By means of this



device the speed of injection of blood could be so regulated that the venous pressure remained within the normal range; on occasion a rate of injection as slow as 4 ml. per minute was necessary. It is suggested that this addition to the accepted technique for exchange transfusion will be especially valuable when treating very anaemic babies.

R. M. Todd 212. Pathways of Fetal and Early Neonatal Infection: Viral Placentitis, Bacterial and Fungal Chorioamnionitis. [Review Article]

W. A. Blanc. Journal of Pediatrics [J. Pediat.] 59, 473-496, Oct., 1961. 23 figs., bibliography.

213. Ventilatory Failure and Right-to-left Shunt in Newborn Infants with Respiratory Distress

L. B. STRANG and M. H. MACLEISH. Pediatrics [Pediatrics] 28, 17-27, July, 1961. 7 figs., 24 refs.

The disordered cardiopulmonary function observed in newborn infants with respiratory distress was studied in 7 infants at Hammersmith Hospital, London. The oxygen and carbon dioxide concentrations in arterial blood were measured in samples obtained through a catheter passed up the umbilical artery into the iliac artery. Reliable samples of mixed venous blood could not be obtained from umbilical vein catheterization, and calculated figures were used for venous blood. The effect of breathing oxygen for 20 minutes was noted.

Evidence was gained of right-to-left shunts, the magnitude of which ranged from 30% to 80% of the total cardiac output. The sites of these shunts were probably the ductus arteriosus and the foramen ovale. Reduced alveolar ventilation attributable to atelectasis was also observed. An inverse relationship was noted between the size of the shunt and the degree of reduction of ventilation. Measurement of the pH of arterial blood revealed considerable respiratory acidosis.

Of the 7 infants, 5 died; at necropsy it was found that 4 had pulmonary hyaline membrane and 2 had in addition intracranial haemorrhage.

J. A. Cosh

214. The Electrocardiogram in the Respiratory Distress Syndrome and Related Cardiovascular Dynamics

J. D. KETTH, V. ROSE, M. BRAUDO, and R. D. ROWE. Journal of Pediatrics [J. Pediat.] 59, 167–187, Aug., 1961. 12 figs., 45 refs.

The electrocardiogram has proved most useful in investigating the dynamics of congenital heart disease. In the present study, carried out at the Hospital for Sick Children, Toronto, the authors have found that it may be of value in the diagnosis and prognosis of the respiratory distress syndrome of newborn infants, and by reflecting the pulmonary dynamics it may be helpful in assessing the response to various therapeutic measures. In this condition the ductus arteriosus is usually widely patent, while pulmonary vascular resistance may be either increased or decreased. High resistance is characterized by a tall R wave over the right precordium and low resistance by a deep S wave in the same region. Infants with the former type usually have a better prognosis and less frequently present with severe distress and hyaline membrane formation. However, infants with low pulmonary vascular resistance and the pattern of left ventricular volume loading (deep S wave in Lead VI) may rapidly revert to normal with closure of the ductus.

The distress syndrome is in most cases related to immaturity of the newborn infant. The probable responsible factors are discussed in full, and it is suggested that

the incidence of the syndrome will diminish as more attention is paid to anoxia, trauma, and other birth difficulties. Therapeutic measures include administration of oxygen and glucose solution, correction of the blood pH as required, and assisted respiration.

T. Semple

CLINICAL PAEDIATRICS

215. A Critical Evaluation of Renal Biopsy in Children N. N. LITMAN, C. L. YUILE, H. LATTA, D. GLICKLICH, and F. G. SMITH JR. American Journal of Diseases of Children [Amer. J. Dis. Child.] 102, 321-343, Sept., 1961. 14 figs., bibliography.

The authors present, from University of California School of Medicine, Los Angeles, a critical study of the practical usefulness of renal biopsy in children in the light of the results in 50 children who were subjected to percutaneous renal biopsy. Intravenous pyelograms were used to locate the site of the biopsy in those cases in which the kidneys were not clearly visualized in the plain radiograph of the abdomen. Specimens for light microscopy were fixed in "technicon" fixative and stained with periodic-acid—Schiff stain (P.A.S.) and with hematoxylin and eosin for electron microscopy; the first 2 to 3 mm. of the cortical end of the biopsy specimen was cut and fixed in osmic acid.

There were no serious complications, but of those which did occur the chief was gross haematuria, which occurred in 2 cases and which was attributable to the patient's struggling during the procedure; delayed bleeding, as reported by other investigators, was not encountered in any instance. In each case a clinical diagnosis was made before performing biopsy and this was compared with the pathological diagnosis. The clinical diagnoses included glomerulonephritis, idiopathic nephrosis, miscellaneous types of the nephrotic syndrome, ill-defined proteinuria, and renal tubular defects; in several cases no clinical evidence of renal disease was found. In general the diagnoses by the two methods showed good correlation.

. Microscopy revealed one case in which renal disease was not suspected and in which there was periarterial adventitial fibrosis of undeterminable actiology, and one case of acute post-streptococcal glomerulonephritis and severe oliguria in which biopsy revealed early subacute nephritis. The microscopic findings were normal in 9 children with idiopathic nephrosis in clinical remission who had been receiving adrenal steroid therapy; in 5 of these cases relapse occurred within one year of discontinuation of steroid therapy. In 2 cases of nephritis associated with lupus erythematosus and 2 of anaphylactoid purpura the pathological findings by light microscopy were indistinguishable from those of chronic glomerulonephritis and examination by electron microscopy did not help in the differentiation of these cases. The 5 cases of ill-defined proteinuria showed a variety of renal

The greatest value of renal biopsy was the help it gave in the histological differentiation of cases of "pure" nephrosis from those of mixed type at an early stage of the disease when the clinical signs were equivocal. Electron microscopy was not found to be of much clinical value in the diagnosis or as a guide to the treatment of any of the renal disorders included in this series. From these experiences the authors conclude that renal biopsy should not be used as a routine laboratory procedure.

R. G. Meyer

216. Dissociation of Growth-stimulating and Skeleton-maturing Actions of the Synthetic Androgen, Fluoxymesterone

W. A. Relly and G. S. Gordan. *Journal of Pediatrics* [J. Pediat.] **59**, 188–193, Aug., 1961. 3 figs., 11 refs.

At the University of California School of Medicine, San Francisco, 16 prepubertal children, short because of familial short stature (11 cases), gonadal dysgenesis (3 cases), delayed puberty (1 case), or hypopituitarism (1 case) were studied for 6 to 41 months (average 15.9 months) while under treatment with fluoxymesterone, a 17-alpha alkylated steroid, in a dose usually of 5 mg. daily by mouth. The drug appeared to be the first androgenic derivative to produce linear growth comparable with that obtained with other androgens without accelerating epiphysial fusion. No jaundice was observed. The average growth rate was 3.2 inches (8.1 cm.) per year, while skeletal age advanced an average of 0.83 year per year. Phallic or clitoric enlargement was the only androgenic effect observed. It is concluded that the combination of growth production and relatively slow skeletal maturation increases the adult height predicted.

R. S. Illingworth

217. Delayed Maturation in Development

R. S. ILLINGWORTH. Journal of Pediatrics [J. Pediat.] 58, 761-770, June, 1961. 13 refs.

218. Clinical Features, Treatment, and Prophylaxis of Residual Psychic Disturbances after Tuberculous Meningitis in Children. (Клиника, терапия и профилактика остаточных психических нарушений после тубериплевного менингита у летей)

M. I. LAPIDES. Журнал Невропатолскии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1077–1082, No. 7, 1961. 26 refs.

Psychological investigations were carried out on 405 children discharged from the First Paediatric Hospital, Moscow, after treatment for tuberculous meningitis during the period 1947-55 and followed up for periods of 3 to 11 years. Treatment in the year 1947 consisted only in the intrathecal injection of streptomycin, but this was supplemented during the period 1948-51 by the intramuscular injection of streptomycin and oral administration of PAS. Latterly, isoniazid was also given by mouth.

Of the 405 patients, 222 showed no abnormality on discharge; the remaining 183 were classified according to the predominant psychological syndrome and clinical picture. Permanent intellectual impairment was found in 20 and epilepsy occurred in 36. A dynamic disturbance of intellectual activity was seen in 53 patients, variously expressed as a weakening of initiative, brady-

phrenia, and psychic infantilism. In 24 cases there was a syndrome of asthenia and in 9 neurotic developments. Disturbances of behaviour such as general motor disinhibition and psychopathic-like behaviour accounted for the remaining 41. The author considers this classification important for an understanding of the mechanisms involved in individual cases and as a guide to treatment. Thus in the case of psychic infantilism the intellectual activity of the patient is disturbed because of his impatience, thirst for new experiences, and constant striving for pleasure. In contrast, the patient with bradyphrenia thinks and acts slowly, but can, given time, undertake tasks appropriate to his age. Patients suffering from the syndrome of weakened intellectual activity and initiative are unproductive because of narrowing of mental outlook. The syndrome of asthenia is characterized by fatigue, restlessness, and lack of self-confidence. Patients suffering from disturbance of behaviour are handicapped either by fussiness and aimlessness of movement or on the other hand by sharp affective explosions. It is felt that these syndromes tend to be distinguished from the residual effects due to other forms of meningoencephalitis by the frequency of the above features.

Of the 183 who originally showed residual psychic effects. 73 have now practically recovered. Factors which favoured the development of residual disturbances were early age of onset, late commencement of treatment. the less efficient treatment methods of earlier years, the presence of miliary spread, and occurrence of psychic upsets in the acute and subacute phases of the illness. Treatment, although varied according to the basic syndrome, was mainly non-specific and consisted in physiotherapy, sport, and pedagogic measures supplemented in selected cases by intramuscular vitamin B₁₂, oral calcium, intravenous infusions of sodium bromide, and neuroplegic drugs. Prophylaxis consisted in sending the majority of convalescent children to sanatoria and subsequently the avoidance of undue fatigue.

G. P. McGovern

219. The Clinical and Virological Characteristics of Isolated Facial Nerve Lesions in Children. (К клиниковирусологической жарактеристике изолированных порачений лицевого нерва у детей).

E. I. Jampol'skaja and E. S. Zalmanzon. Журнал Невропатоловии и Психиатрии [Ž. Nevropat. Psihiat. 161. 967-972, No. 7, 1961. 1 flg.

A study was made of 115 children admitted to the Clinic for Infectious Diseases of the Nervous System, the Paediatric Institute, Moscow, during 1958 and 1959 suffering from an isolated lesion of the facial nerve. Three samples of faeces were taken during the first few days after admission. Three specimens of venous blood were taken, on admission, after 10 to 14 days, and before discharge respectively. In selected cases the cerebrospinal fluid was examined. In every case tests were made for poliomyelitis virus and for Coxsackie viruses B2, B3, B4, B5, and A9. Of those cases originally diagnosed as poliomyelitis, this was confirmed in only 34.5%. Only one case not so diagnosed was later found to be a case of poliomyelitis. On completion of the investigation the patients were divided into three groups, namely,

poliomyelitis, typical facial neuritis, and paralysis of the facial nerve without sensory disturbance.

Of 20 patients with confirmed poliomyelitis, twothirds were aged 2 years or less. Most had fever and some systemic disturbance, and in 13 the cerebrospinal fluid showed increase of pressure and pleocytosis. All the patients either excreted poliomyelitis virus in the faeces or showed a 4- to 8-fold increase in antibody titre. Only 5 had any residual lesion when discharged from hospital.

There were 53 patients with a clear picture of facial neuritis and of these, 42 were aged 8 years or older. The neuritis usually developed suddenly without rise of temperature. Subjectively, there was earache, toothache in the lower jaw, and hyperaesthesia of the affected side. Objectively, there was, in addition to paralysis, diminished cutaneous sensation of the face and diminished taste sensation on the anterior two-thirds of the tongue on the affected side. In 3 cases the neuritis was connected with a lesion of the middle ear. In 3 cases Coxsackie virus was isolated, but without rise in antibody titre. In 6 cases there was a rise in poliomyelitis antibody titre, but this was insufficient for a diagnosis of poliomyelitis to be made. In 13 cases there was a four- to eightfold increase in influenza virus antibody titre, but the aetiological link was thought to be uncertain in view of the frequency of coincidental symptomless

There were 42 cases of paralysis without disturbance of sensation which, the authors consider, represented a special category of facial nerve lesion of unknown actiology. In all these cases the temperature and cerebrospinal fluid were normal and in 35 of them virus and serological studies were negative. Four patients either yielded poliomyelitis virus or showed an increase in antibody titre and in 3 cases there was an increase in Coxsackie virus titre. G. P. McGovern

220. Infantile Muscular Atrophy R. K. Byers and B. Q. Banker. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 140-164, Aug., 1961. 9 figs., 23 refs.

After a historical review of infantile muscular atrophy. the authors describe their experience of 52 cases of the disease seen by them over an 11-year period at the Chil-. dren's Hospital Medical Center, Boston, Massachusetts. They found that because of a variation in the intensity of the basic disease of the anterior horn cells there was a resultant variability in the clinical picture. Certain muscles, including the diaphragm and extraocular muscles, always escaped clinical involvement. The distal muscles of the extremities appeared stronger than the proximal muscles. Weakness was often apparent in the bulbar musculature as the disease progressed. The most severely affected muscles were always those of the limb girdles and trunk. The genetic nature of the disease was evident; the corrected figures of incidence support the concept that the disease is transmitted by an autosomal recessive gene. There is no specific treatment.

. Hugh Garland

Medical Genetics

221. Genetics of Convulsive Disorders. II. Genetic and Electroencephalographic Studies in Centrencephalic Epilensy

K. Metrakos and J. D. Metrakos. Neurology [Neurology (Minneap.)] 11, 474-483, June, 1961. I fig., 10 refs.

In the first part of this study (Neurology (Minneap.), 1960, 10, 228; Abstr. Wld Med., 1960, 28, 414) children with convulsive disorders were defined as those who had a history of at least one convulsion irrespective of cause; from that study it was concluded that the relatives of affected children included a higher proportion of affected persons than did the relatives of unaffected children. The authors drew attention to the limitations of their data and to the heterogeneous nature of the affected propositi. In this further study the affected propositi were limited to children with "typical or atypical centrencephalic epilepsy". On this basis 211 affected propositi were selected from the Montreal Children's Hospital, all of whom had a history of recurrent petit and/or grand mal seizures "with no obvious neuropathology to account for their seizures, and a centrencephalic electroencephalogram". For controls, 112 propositi were obtained by examining the record of every twentieth patient admitted to the same hospital and including the patient in the study if there was no history of convulsions, no neuropathological illness, and the electroencephalogram (EBG) was within "normal or borderline normal limits". The two groups showed no significant differences in regard to age of parents, ethnic origin, socio-economic status, size of sibship, and parity [details are shown only for the last], but the sex ratios were very different, the proportion of boys being 49% in the affected group compared with 65% in the control group; it is stated, however, that the latter figure was more nearly representative of the sex distribution in the over-all hospital population.

Information about age, medical history, cause of death, and convulsive disorders was obtained for 7,377 relatives of affected children and 4,026 relatives of the controls. [How this was obtained and what proportion of the possible total these figures represent are not stated.] For each degree of relationship, parents, sibs, aunts and uncles, grandparents, and cousins the proportion of subjects with a history of at least one convulsion was greater among relatives of the affected children than among those of the controls; these proportions were respectively 13.51 and 1.34% for parents, 12.72 and 4.66% for sibs, 4.20 and 3.13% for aunts and uncles, 2.61 and 0.67% for grandparents, and 1.46 and 0.66% for cousins. [It would have been of interest to know if age affects any of these comparisons.]

EEG examinations were carried out on 195 parents and 223 sibs of affected propositi and 84 parents and 103 sibs of control propositi. The results are given in detail

and it is of particular interest that 15 (7.69%) of the parents of affected propositi had centrencephalic abnormality compared with only 3 (2.38%) of the parents of controls; the corresponding figures for sibs were 82 (36.77%) and 9 (8.74%). A table showing the proportion of parents and sibs of affected propositi with such abnormality in successive age groups suggests that age has an important role in determining the presence of the EEG trait. Thus 25.4% of the sibs under age 4½ years had the trait compared with about 44% in the age group 41 to 81 years and 22% in those aged 161 to 201 years, and although the numbers of parents are rather small, the observed proportions suggest a downward age trend to possibly zero by about the age of 40 years. On the basis of these observations the authors conclude that "the centrencephalic type electroencephalogram is the expression of an autosomal dominant gene, with the unusual characteristic of a very low penetrance at birth, which rises rapidly to nearly complete penetrance for ages 41 to 161 years and declines gradually to almost no penetrance after the age of 40½ years".

[Although the authors' results may be compatible with their conclusion, this type of analysis cannot be fully convincing. Family studies are essential and it is to be hoped that these may appear later, since presumably some pedigree data must be available from the work already carried out. In the present analysis it is possible that some families with affected members are included in their entirety whereas others are not, and some of the affected propositi presumably have an affected parent while others have not. The apparent influence of age on penetrance raises several difficulties, in this and in familial studies, which may be impossible to overcome without very long-term prospective studies of affected children and their sibs.]

222. On the Genetics of the Gm Serum System. [In English]

B. Brandtzeg and J. Mohr. Acta genetica et statistica medica [Acta genet. (Basel)] 11, 111-125, 1961. 11 refs.

The original Gm serum system, with a basic dichotomy represented by two allelic genes Gma and Gmb diagnosable by specific antisera, was further subdivided by the discovery by Harboe and Lundevall of the factor Gmx, which appeared to be related to Gma, the specific antiserum reacting exclusively with serum from individuals possessing Gm(a). The serum anti-Gm(x) thus appeared to differentiate Gm(a) into two subtypes in a way analogous to the differentiation of A in the ABO blood group system into the subtypes A₁ and A₂. However, this analogy may be misleading, since Gm(x) has subsequently been found in an individual who lacks Gm(a). With inhibition tests and the specific antisera for Gm(a), Gm(b), and Gm(x), it is possible to distinguish phenotypes such as Gm(abx), Gm(abx), or Gm

(abx), the bar meaning absence of the factor and the unmarked letter its presence.

A study of 199 unrelated Norwegians revealed, 121 Gm(a) individuals, of whom 36 were Gm(abx), 18 Gm(abx), 60 Gm(abx), and 7 Gm(abx). In none of the 78 Gm(a) persons was Gm(x) present and no person was found of the type $Gm(\overline{a}b\overline{x})$. In a total of 482 individuals typed (including various family studies carried out by the authors and others and 119 unrelated individuals typed by Harboe) no person of type Gm(ax) was found. In studies made by the present and other authors of a total of 51 families of the mating type. Gm(a) × Gm(a) none of the 146 children were found to be Gm(a). In a further 52 families studied for Gm(a), Gm(b), and Gm(x) each character behaved as a simple dominant and neither in this study nor in those previously published was there abnormal segregation of the Gm(a) genes.

When all three types—Gm(a), Gm(b), and Gm(x)—are used the Gm system has a usefulness in problems of identity, calculated according to Fisher, of 33.3%, in the diagnosis of zygosity of twins of 58.34%, and in disputed paternity of 72.72%.

I. Dunsford

223. The Gm (r) Serum Group. [In English]
B. Brandtzeg, H. Fudenberg, and J. Mohr. Acta genetica et statistica medica [Acta genet. (Basel)] 11, 170–177, 1961. 10 refs.

To the existing hereditary serum γ -globulin groups Gm(a), Gm(b), and Gm(x) has been added another, Gm(r). It is related to the Gm(a) group in that it was present in 173 of 193 Gm(a) persons studied and absent in 130 Gm(a) individuals. In 95 families with 348 children studied the inheritance of Gm(r) appeared to be that of a simple dominant.

The serum γ -globulin levels, measured by a modified zinc turbity reaction, showed no significant differences in the three types Gm(ar), $Gm(\overline{ar})$ and $Gm(a\overline{r})$. Electrophoresis and ultracentrifuge studies revealed that Gm(r), as well as Gm(a), Gm(b), and Gm(x), was confined to the 7S γ globulin.

I. Dunsford

224. Nucleolus-organisers in the Causation of Chromosomal Anomalies in Man

S. OHNO, J. M. TRUJILLO, W. D. KAPLAN, and R. KINOSITA. *Lancet* [*Lancet*] **2**, 123–126, July 15, 1961. 6 figs., 12 refs.

This paper from the City of Hope Medical Center, Duarte, California, reports observations on interphase and prophase nuclei in foetal liver cells and on metaphase preparations of cultured peripheral blood leucocytes from normal and leukaemic individuals. The authors agree with Ferguson-Smith and Handmaker (Lancet, 1961, 1, 638; Abstr. Wld Med., 1961, 30, 252) that the short arms of all five pairs of acrocentric chromosomes (Nos. 13, 14, 15, 21, and 22) may carry satellites. In any one metaphase preparation no more than 6 chromosomes have been seen to have satellites. The special relationship of the satellited chromosomes to the nucleolus was confirmed by study of nuclei at interphase and early prophase. The greatest number of nucleoli seen

was 6, but most nuclei had only one. This tendency of nucleoli to coalesce is important in bringing together the satellited chromosomes.

The satellite association of acrocentric chromosomes in metaphase preparations [described by Penrose and Harnden (Recent Advances in Human Genetics, London, 1961), and by Ferguson-Smith and Handmaker (op. cit.)] has been studied in cases of chronic myeloid leukaemia in which the Philadelphia (Ph1) chromosome could be seen. Cells with a Ph1 chromosome are said seldom to contain chromosomes showing satellite association. In one case of chronic myeloid leukaemia a correlation is reported between the smallness of the Ph1 chromosome and an increase in length of the short arm of chromosome No. 14 or 15. This observation suggests that in this case the Ph1 chromosome arose as a result of a reciprocal translocation. This and other examples of chromosome breakage and aberrant reunion-some described and some as yet hypothetical—are discussed. A scheme for their origin as a result of the special relationship of satellited chromosomes and the nucleolus is suggested. A. G. Baikie

225. Recent Progress in Human Chromosome Analysis and Its Relation to the Sex Chromatin

A. R. SOHVAL. American Journal of Medicine [Amer. J. Med.] 31, 397-441, Sept., 1961. 10 figs., bibliography.

226. Chromosomal Aberrations in Human Disease: a Review of the Status of Cytogenics in Medicine

K. HIRSCHHORN and H. L. COOPER. American Journal of Medicine [Amer. J. Med.] 31, 442-468, Sept., 1961. 16 figs., bibliography.

227. Chromosomal Aberrations in Man. [Review Article]

S. RAPPOPORT and W. D. KAPLAN. *Journal of Pediatrics* [J. Pediat.] 59, 415-438, Sept., 1961. 4 figs., bibliography.

228. Studies of Alcaptonuria: a Genetic Study of 58 Cases Occurring in Eight Generations of Seven Interrelated Dominican Kindreds

R. A. MILCH. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 131-136, April, 1961. 3 figs., 15 refs.

In this communication from Johns Hopkins University School of Medicine, Baltimore, the author discusses an extensive pedigree of a number of interrelated kindreds investigated in the Dominican Republic which showed the segregation of alkaptonuria, a total of 58 authenticated cases having been discovered. It is suggested that the familial distribution is consistent with autosomal recessive inheritance and that there is no necessity to postulate dominance.

H. Harris

229. Familial Renal Tubular Acidosis

R. E. RANDALL JR., and W. H. TARGGART. Annals of Internal Medicine [Ann. intern. Med.] 54, 1108-1116, June, 1961. 2 figs., 40 refs.

Study of a family in which at least seven members have renal tubular acidosis suggests that the underlying defect in renal function is determined by an autosomal dominant gene.—[Authors' summary.]

Public Health and Industrial Medicine

230. Poliomyelitis-like Disease in 1959

A COMBINED SCOTTISH STUDY. British Medical Journal [Brit. med. J.] 2, 597-605, Sept. 2, 1961. 11 refs.

During the summer of 1959 an unusual epidemic situation was observed in Scotland: although many patients were being admitted to hospital with the provisional diagnosis of "poliomyelitis" or "meningitis", no poliomyelitis virus was isolated. A report is presented on 310 cases of such "poliomyelitis-like illness" from a large part of Scotland, including the Clyde Valley, Dundee, and Edinburgh.

Clinically, these cases were grouped into three categories: (a) those in which muscle paralysis was a feature (13); (b) those in which there was no paralysis, but features of meningitis (271); and (c) those not fitting into the above categories (26). Virological and other investigations were carried out in all but 20 cases, 174 infections, being identified in 168 patients. Three main virus agents were encountered: Coxsackie A7, Coxsackie B5, and Frater virus; these accounted for 116 of the 174 infections. Other infections were due to mumps virus, E.C.H.O. viruses, leptospirosis, other Coxsackie viruses, adenoviruses, herpes simplex virus, louping-ill virus, and poliomyelitis virus Type 1. Over the whole series males outnumbered females by 2:1, and only 84 of the patients were over 15 years of age. These predominantly childhood infections occurred mainly between May and October inclusive. There was evidence of epidemic grouping of cases of infection by Coxsackie A7 and Frater viruses; paralysis was associated with both these organisms. One death occurred in a child with Coxsackie A7 infection after a brief paralytic illness. Summaries of cases are included in the paper to illustrate the various types of infection.

This study, in which a viral cause was identified in over one-half of cases of "aseptic meningitis", has high-lighted the virtual disappearance of poliomyelitis virus in Scotland in 1959 and has thrown into prominence cases of paralysis due to other viruses, such as Coxsackie A7.

John Fry

231. Interference Patterns Encountered when Using Attenuated Poliovirus Vaccines

J. H. HALE, L. H. LEE, and P. A. GARDNER. British Medical Journal [Brit. med. J.] 2, 728-732, Sept. 16, 1961. 8 figs., 10 refs.

During the course of two trials with attenuated poliovirus oral vaccines, one in Singapore during an epidemic due to Type-1 poliovirus and the other in Newcastle upon Tyne, the authors took the opportunity of observing any interference effects between the vaccine strain, the epidemic strain, and other enteric viruses. In Singapore, where a Sabin Type-2 poliovirus vaccine was given, no infection with the Type-1 epidemic strain was detected in any of the vaccinated children between 8 and 19 days after vaccination; in 8 instances before the eighth day

previous infection with the epidemic strain prevented colonization of the vaccine strain.

In Newcastle three groups of children were treated by different vaccination schedules: (I) one dose of vaccine of each of the 3 virus types simultaneously; (II) as above, but the dose repeated twice more at monthly intervals; and (III) each type given alone at monthly intervals, the order being Type 1, Type 3, Type 2. In Group I five distinct patterns of response were observed. Administration of the 3 types in a single dose often resulted in failure of production of antibodies to Types 1 or 3, or to both, but antibodies to Type 2 were always produced. In Group II the same five patterns were seen after the first dose, but subsequent doses allowed colonization of the intestine by the types that were interfered with at the first dose. In Group III the vaccines given sequentially generally produced infection of the gut, and antibody responses to all 3 types resulted, but a few instances were observed of one virus type becoming so well established that it interfered with the establishment of the next type a month later. To avoid this kind of interference the interval between doses should probably. be extended to 6 to 8 weeks.

Enterovirus infections existing at the time of vaccination in some instances interfered with the establishment of a poliovirus infection, but whether this occurred depended on the stage of the existing infection. The converse was also found to be true.

A. Ackroyd

232. Results of a French Survey on the Role of Tobacco, Particularly Inhalation, in Different Cancer Sites

D. SCHWARTZ, R. FLAMANT, J. LELLOUCH, and P. F. DENOIX. Journal of the National Cancer Institute [J. nat. Cancer Inst.] 26, 1085–1108, May, 1961. 13 refs.

The results of a retrospective study of the smoking habits of 3,937 patients with cancer admitted to hospitals in Paris and a number of provincial cities in France are presented. Each of these patients was matched with 2 control (non-cancerous) patients, one from a general medical ward and one admitted to hospital for an industrial or traffic accident. Matched patients were in the same 5-year age group and were interviewed by the same person; all were male. The total number of controls was 3,614. "The control group was not twice the number of the cancer group, because each pair of controls served for several different cancer sites."

A comparison of the smoking habits of the two control groups showed several similarities, but the patients from a general medical ward had smoked a little more than the other group and a greater proportion of them inhaled. The greater proportion of inhalers was characteristic only of certain diseases (for example, arteriosclerosis), so that the medical patients were thought, as a group, to be unrepresentative of the healthy population. This group was therefore excluded as a control and the patients with cancer were compared only with the group

of accident cases. The patients with cancer differed from their controls in respect of area of residence, family, situation, and occupation. These factors had very little influence on smoking habits, and it is shown that they can be ignored. The main characteristics studied—method of smoking, quantity smoked, and inhalation—were interrelated, and this interrelationship must be taken into account in interpreting the findings.

The sites of cancer which showed no association with smoking (stomach, intestine and rectum, skin, kidney, prostate, and various other sites) also showed no important association with any of the individual smoking characteristics. The sites associated with smoking fell into two groups: (1) cancer of the lung, larynx, and bladder; and (2) cancer of the lips, tongue, rest of oral cavity, oropharynx, hypopharynx, and oesophagus. The patients in both these groups smoked, on an average, more than their controls; but in the first group the cancer patients smoked cigarettes more often and inhaled more often than their controls, whereas these differences were absent in the second group.

Among patients with cancer of the lung it was found that there was a higher proportion of cigarette-smokers than of pipe-smokers among both those who inhaled and those who did not. There was also a higher proportion of smokers of cigarettes only than of smokers of both cigarettes and pipe at each level of smoking, which cannot wholly be accounted for by differences in inhalation. As compared with the controls the proportion of inhalers was higher among the patients with lung cancer at smoking levels of under 10 cigarettes a day, 10 to 19 a day, and 20 to 29 a day, but the difference diminished with increasing numbers of cigarettes smoked, so that at 30 and more a day the difference became (non-significantly) negative.

The association between lung cancer and chronic bronchitis was confirmed. Chronic bronchitis was associated with inhaling, but this could not explain the whole of the association with lung cancer.

Richard Doll

233. Influence of the Weather on Respiratory and Heart Disease

W. W. HOLIAND, C. C. SPICER, and J. M. G. WILSON. Lancet [Lancet] 2, 338-341, Aug. 12, 1961. 19 refs.

The authors examined by multiple regression coefficients the statistical relationship between certain causes of admission to hospital through the Emergency Bed Service, London, and to sick quarters of the Royal Air Force and certain meteorological variables, including barometric pressure, temperature, humidity, rainfall, sunshine, and air pollution with smoke.

No significant correlations were found between the meteorological conditions and admissions for heart disease, but correlations "on the edge of statistical significance" were found between admissions for respiratory disease and "atmospheric pollution and inversely for temperature". It is concluded that the evidence indicates "that both atmospheric pollution and low temperature have an effect on the admissions to London hospitals of patients aged more than 15 years with acute respiratory disease".

John Pemberton

234. Viricidal Efficiency of Disinfectants in Water P. W. Kabler, N. A. Clarke, G. Berg, and S. L. Charg. Public Health Reports [Publ. Hlth Rep. (Wash.)]. 76, 565-570, July; 1961. 1 fig., 29 refs.

Data from recent studies of the efficiency of various disinfectants in inactivating enteric viruses in water appear to support the following summarizations: Different types of enteric viruses vary widely in the degree of resistance to free chloride. Poliovirus, Coxsackie, and some ECHO viruses seem to be more resistant than coliform or enteric pathogenic bacteria. The free chlorine residuals required for inactivation depend on pH, temperature, and contact time. Combined chloride is considerably less viricidal than free chlorine, requiring higher concentrations or longer contact periods to achieve comparable inactivation. Iodine is an effective viricide, but requires greater residuals and longer contact than hypochlorous acid. Chlorine dioxide, ozone, and ultraviolet light may be useful disinfectants; however, their efficiency in water in comparison with that of free chlorine and the quantitative effects of pH and temperature have not been established. - [Authors' summary.]

INDUSTRIAL MEDICINE

235. Effects of Infective Bronchitis on Respiratory Function in Silicosis. (Effetti della bronchite infettiva sul quadro funzionale respiratorio della silicosi)
E. GAFFURI, A. BERRA, and A. REGGIANI. Medicina del lavoro [Med. d. Lavoro] 52, 271-279, April [received Sept.], 1961. 13 refs.

Writing from the Institute of Industrial Medicine, University of Padua, the authors point out that since infection of the respiratory tract plays an important part in aggravating and tending to make chronic such conditions as bronchitis and emphysema, it may well be one of the factors responsible for the lack of relationship between the x-ray appearances and the incidence and gravity of these diseases in miners. Hence a comparison of two groups of patients with chronic bronchitis, not differing significantly in x-ray appearances or deficit of respiratory function, but differing only in that one has and the other has not infective bronchitis, is best made by observing the results of anti-infective treatment, the criterion of infective bronchitis being the presence of purulent sputum. Such a test was therefore carried out on 18 patients, all of whom had been miners for a number of years and most of whom had been exposed to rock dust or other mineral dusts; all had chronic bronchitis (10 with emphysema) and 9 had infective bronchitis in addition, the diagnosis of the latter being based on a daily amount of sputum of more than 20 ml., 50% of which was purulent. The degree of silicosis (Geneva classification) was similar in both groups. Treatment was not identical in the two groups, but in both it was based on anti-infective measures, mainly chloramphenicol, and the administration of oxygen, bronchodilator drugs, and respiratory detergents, a trypsin-chloramphenical aerosol being used in cases with dense purulent. sputum.

In the patients with infective bronchitis there was a marked reduction in the amount of sputum and an almost total disappearance of the pus in it, this being accompanied by considerable improvement in the maximum. expiratory volume, vital capacity, and arterial blood oxygen saturation. In patients without infective bronchitis only the vital capacity was improved and then only to about half that in the infective group. The authors conclude that the fact that the patients with infective bronchitis showed improvement in pulmonary function after treatment shows that their initial identity with the non-infective group may be only temporary. They consider that repeated exacerbations of infection are important in the development of chronic respiratory deficiency in such patients. W. K.: Dunscombe

236. Treatment of Chronic Bronchitis in Silicotics with a New Nitrofuran Preparation. (Terapia della bronchite cronica dei silicotici con un nuovo preparato nitrofuranico)

L. PARMEGGIANI and E. SAVOLDI. *Medicina del lavoro* [*Med. d. Lavoro*] **52**, 280–294, April [received Sept.], 1961. 5 figs., 16 refs.

The authors report from the Clinic of Industrial Medicine, Milan, a trial of a new nitrofuran, 5-morpholino-3-(5-nitrofurfurylideamino)-2-oxazolidinone (MNO), which has been shown in vitro to exhibit less of a tendency to induce drug resistance in Staphylococcus aureus than, for example, erythromycin. The trial was carried out on 25 patients with chronic bronchitis, of whom 21 had in addition silicosis, one emphysema, 2 bronchiectasis, and one asbestosis. The drug was given in a dosage of 8 to 29 mg. per kg. body weight daily divided in 4 doses, with meals, for varying periods up to 30 days.

There was a marked reduction in the amount of sputum in 17 (70%) of the patients, with reduced turbidity and number of pus cells. Bacteriologically, 10 (40%) showed a reduction in the numbers of organisms, especially Gram-positive bacteria (pneumococci and staphylococci), while clinically 50% showed improvement, the condition clearing up completely in 2 cases. No haematotoxic effects from the drug were seen. Follow-up by questionary in 19 cases showed that in one case there was no relapse after 14 months and in 2 none after 4 months. Relapse occurred in one case after 8 months and in 4 cases in 3 months or less. In the remaining 16 cases the time elapsed was too short for any conclusions to be drawn. A full description is given of the 3 cases which showed the most improvement, but the authors state that the results with this drug are generally better when the bacterial flora is entirely or mostly Grampositive, although they may be good even when Haemophilus (Gram-negative) predominates. Dosage is the fundamental factor, the optimum dosage being 25 mg. per kg. daily (6 or 7 tablets) for 12 to 15 days. The sideeffects were by no means negligible, though they were much greater when the customary wine was taken with meals. MNO is contraindicated in gastro-duodenal ulceration or chronic inflammation and in patients with hypertension, marked arteriosclerosis, or blood diseases. Repetition of the treatment when this is deemed necessary

does not seem to produce resistance in the bacterial flora usually present in sputum.

The authors therefore consider the results obtained with MNO very encouraging in this class of case, but abstention from alcohol during treatment and administration of the drug during or immediately after meals are advisable. They suggest that if its efficacy is also proved elsewhere the drug may be found useful as a prophylactic measure, especially for the prevention of recurrences of winter bronchitis.

W. K. Dunscombe

237. Treatment of Respiratory Insufficiency in Emphysema and Silicosis. (Terapia dell'insufficienza respiratoria negli enfisematosi e nei silicotici)

E. SARTORELLI. Medicina del lavoro [Med. d. Lavoro] 52, 295-304, April [received Sept.], 1961. 5 refs.

In the last 10 years the increasing number of patients with emphysema or silicosis attending the Clinic of Industrial Medicine, Milan, has furnished the author with a special opportunity to study the treatment of respiratory insufficiency in patients with pulmonary diseases, and in this paper he describes the methods used and the results obtained in several hundred such patients. Of the pathological lesions associated with chronic obstructive pulmonary emphysema; the chief is bronchiolar obstruction with chronic bronchial inflammation, the causes of which are multiple and comprise toxic, infective, and allergic agents. The methods of diagnosis include the usual clinical and laboratory tests, recording of the electrocardiogram, testing of the bacterial flora for sensitivity to antibiotics, complete x-ray examination (with fluoroscopy, tomography, and bronchography if required), a full study of respiratory function, and in special cases investigation of the pulmonary vascular flow by cardiac catheterization.

Treatment consists in the administration of (1) oxygen by intermittent positive pressure through an oro-nasal mask for 20-minute sessions usually 3 times a day for periods varying from 16 to 126 days; (2) bronchodilator drugs, an aerosol of either racemic or L-isopropylnoradrenaline plus chloramphenicol succinate or glycinate, or a penicillin salt of tetracycline being used, depending on the sensitivity of the organism in the sputum; (3) mechanical artificial respiration, which is important in patients with severe carbon dioxide intoxication; and (4) active re-education of respiratory function, for which the exercises employed are described; some of these involve manipulation of the spine. Treatment with steroids such as prednisone or prednisolone in doses of 40 to 50 mg, per day is useful when there is a marked asthmatic element, while centrally acting analeptics in high dosage are given if there is serious ventilatory insufficiency; pulmonary hypertension is treated with aminophyllin, reserpine, or promazine and cor pulmonale with heart tonics and diuretics. In regard to the latter, mercurials have been given up and the drug at present favoured is chlorthalidone in a dosage of 300 to 400 mg. daily.

Between January, 1953, and April, 1961, 478 patients, of whom 371 had chronic bronchitis often of asthmatic type with emphysema of various degrees of severity and 107 had silicosis of varying grades, have been treated,

177 of the total having either very severe or grave respiratory insufficiency (anoxaemia even at rest, hypercapnia, and right heart decompensation). More than 90% of all patients showed improvement, and of the 177 with advanced respiratory insufficiency, only 16 died, a figure which the author claims is very much lower than any others published; 4 of these 16 had a bronchopulmonary infection resistant to antibiotics, 3 paroxysmal ventricular tachycardia, 2 were almost moribund on admission, and in the remaining 7 the treatment failed. Two tables show the improvement in maximum expiratory volume. vital capacity, and oxygen saturation in 184 patients with chronic bronchitis and emphysema and in 42 with silicosis. The author concludes that this combined treatment, which should all be carried out at the same-time. is a rational procedure in patients with such symptoms. W. K. Dunscombe

238. Patch Testing in Dermatitis from the Newer Resins M. M. Key, V. B. Perone, and D. J. Birminoham. Journal of Occupational Medicine [J. occup. Med.] 3, 361–364, Aug., 1961. 18 refs.

Patch test reactions to the newer resins used widely in the rapidly growing plastics industry are complicated by the large number of components of these resins. At the Division of Occupational Health, U.S. Public Health Service, Cincinnati, Ohio, over 600 patch tests were carried out on human volunteer subjects, using concentrations which had previously been found non-irritating to animals, thus providing a useful distinction between allergic sensitivity and primary contact irritation. The recommended concentrations for 10 epoxy resin components, 3 epoxy resin modifiers, 4 polyester resin components, and 8 polyurethane resin components are presented in tabular form, as also are lists of the combination of components used in "curing" epoxy resins and those of polyester resins.

It is concluded that the majority of cases of occupational dermatitis resulting from handling the newer resins are due to primary contact irritation rather than to allergic sensitivity. This contact dermatitis arises most frequently from the amine hardeners or curing agents in epoxy resins, occasionally from the polyester resin components, and rarely from polyurethane components. Allergic sensibility may be caused by uncured amino- and phenolic resins and uncured furanes and by polyester monomer and its modifiers.

Ethel Browning

239. The Use of "Biological Gloves" in Certain Leningrad Factories. (Опыт применения "биологических перчаток" на промышленных предприятиях Московского и Ленинского районов Ленинграда) І.О. Šаріко and V. Ja. Китавнікоv. Вестник Дерматоловии и Венероловии [Vestn. Derm. Vener.] 35, 57–59, June, 1961.

The authors describe a method of protection of workers against industrial dermatitis by the use of so-called "biological gloves". This method was first suggested in 1957, and applied in certain factories from September, 1959, onwards. Among the irritants used in these factories were white spirit, kerosene, and various resins.

The "gloves" consist of a thin film of a solution which is applied to the hands and so prevents the irritants from attacking the skin. The solution consists of casein, ammonium hydrate, glycerin, rectified spirit, and distilled water. The properties and the method of preparing the solution are described. The authors state that since the introduction of this preparation the incidence of industrial dermatitis has markedly decreased. N. Hopewell

240. Chronic Occupational Exposure to Strontium-90 and Radium-226

J. MÜLLER, A. DAVID, M. REISKOVA, and D. BREZIKOVA. Lancet [Lancet] 1, 129-131, July 15, 1961. 4 figs., 3 refs.

During a survey of painters of luminous dials carried out at the Institute of Occupational Diseases, Prague, it was found that the paint being used, which had been described by the manufacturers as harmless and so had not come under the regulations for radioactive substances, contained up to 1.2 mc. of radioactive strontium (90Sr) per g., as well as a small amount of radium. Of 103 workers so exposed, 34 were examined in hospital in detail for urinary excretion of 90Sr and 10 also for body burden of radium, peripheral blood counts and bone marrow examination being carried out in all cases. The urinary test was performed by precipitating the 90Sr as oxalate and determining the β activity of the precipitate after equilibrium was reached between 90Sr and radioactive yttrium (90Yt), a standard of 90Sr+90Yt in equilibrium being used for comparison. The body burden of radium was estimated by a radon breath-sampling method.

The daily urinary excretion of 90Sr in 2 workers examined immediately after stopping this type of work was $10^{-3}\mu c$. per day, decreasing to $10^{-4}\mu c$. per day during the following year. The other 32 patients, first investigated a year or more after cessation of work, showed considerable daily variation in the amount excreted, but there was a decreasing trend with time, except in one case in which this trend was not apparent and another in which, after proved fresh contamination at the patient's home, the excretion had risen to nearly 1 µc. per day. In 2 of the 10 patients examined the body burden of radium was 10⁻⁸ g., but in the remainder it was below this value. Subjective complaints of weakness, headache, sleepiness, and pains in the bones were regarded as mainly "neurasthenic", but it was difficult to determine to what extent ionizing radiation may have played a part. In the remaining 69 workers, examined as out-patients, haematological changes were manifested chiefly in the peripheral blood by signs of initiation of erythropoiesis (reticulocytosis) and in the bone marrow by hyperplasia. of the erythroblast series; in 4 cases normoblasts in the stage of mitosis numbered more than 50 per ml., with basophil stippling, karyorrhexis, and polyploidy. The body burden of 90Sr was calculated from the daily excretion and assumed to be of the order of tens of microcuries. The preventive measures taken have included thorough decontamination of work-places and of the homes and clothes of the workers and establishment of an accurate dosimetric service. Ethel Browning

Toxicology

241. Accidental Poisoning in Children

M. A. Heasman. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 390-393, Aug., 1961. 6 refs.

Analysis of data collected in 1958 by the Hospital Inpatient Enquiry of England and Wales showed that of 1,000 consecutive cases of poisoning, 218 were in children under 15 years of age (138 boys and 80 girls). The author states that while details were only rarely available it seemed fair to assume that in the majority of cases the poisoning resulted from inquisitiveness and was therefore accidental.

Poisoning among children admitted to hospital was most common in those between one and 3 years of age; (it is pointed out that older children, from whom the amount taken can be elicited, tend to be treated without admission to hospital). Almost half the cases were due to ingestion of medicinal pills or tablets, aspirin accounting for most of them, followed by the barbiturates. Iron compounds accounted for 7 out of 105 cases. In 70 of the 218 cases household substances were responsible, paraffin and disinfectants being the most frequent. Rarer substances included brandy, floor polish, moth balls, rat poison, and surgical spirit, each in one case. Poisoning from berries and from plant substances was seen in only 8 cases, laburnum seeds being incriminated in 4 of these.

Discussing deaths of children from poisoning (there were none in the present series) the author states that during the period 1954—8 the mortality remained at about 44 a year, almost half of these deaths being due to coal gas inhalation. The commonest cause of death, where specified, in the remaining cases was aspirin, followed by iron preparations. Deaths in children over the age of 5 were rare.

It is concluded that few cases of poisoning in childhood are severe and hospital admission is often a precautionary measure; at the same time, nearly all are preventable. Aspirin, paraffin, and turpentine accounted for 36% of hospital admissions for poisoning in children and these substances are found in nearly every home. Availability is at least as important as attractiveness and substances unattractive to adults are not necessarily unattractive to children.

Gavin Thurston

242. Diagnosis and Treatment of Acute γ -Benzenehexachloride Poisoning in Young Children. (Diagnose und Therapie der akuten γ -Hexa-chlor-cyclohexan-Vergiftung bei Kleinkindern)

O. STUR and E. ZWEYMÜLLER. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 86, 1474-1476, Aug. 4, 1961. 15 refs.

The authors describe 3 cases of benzene hexachloride poisoning in infants admitted to the University Pediatric Hospital, Vienna, all of which were due to accidental

ingestion of the proprietary insecticide " jacutin ". The first patient, a boy aged 11, ingested 1 to 21 tablets of jacutin. Half an hour later he became restless, started to scream, and developed tonic-clonic convulsions accompanied by jerky eye movements and cyanosis. The child lost consciousness and the pupils became widely dilated. The stomach was washed out repeatedly and 10 ml. of a calcium solution was given intravenously with 10 ml. of lobeline subcutaneously. On admission to hospital the child had depressed muscle tone and tendon reflexes, but the cremaster and abdominal reflexes were normal. Chvostek's sign was absent on the right. An injection of 10 ml. of a 10% solution of calcium thiosulphate was given intravenously and 0.5 ml. of a 20% solution of "luminal" intramuscularly, and within 10 minutes the convulsions abated and the patient began to regain consciousness. One week later he was discharged from hospital.

The second patient was a girl aged 2 years who was admitted to the clinic after swallowing 650 mg. (one tablet) of jacutin. The symptoms and signs were similar to those in the first case although here the reflexes were absent and the pupils reacted only slightly to light; there absent and the pupils reacted only slightly to light; there and the blood pressure 85/45 mm. Hg. Treatment consisted in giving 5 ml. of 10% calcium thiosulphate intravenously and washing out the stomach, while charcoal and magnesium sulphate were given orally. Convulsions ceased after this treatment and half an hour later a further 10 ml. of 10% calcium thiosulphate solution was injected intravenously. The child was discharged 5 days later.

In the third case the patient was a boy aged 1½ years who was found licking a jacutin fumigating candle, a small piece of which was removed from his mouth, but it was estimated that he had swallowed about one-tenth of the candle. Within 15 minutes of ingestion of the poison tonic-clonic convulsions of all limbs began and lasted 5 minutes. The child was treated in a similar manner to the other 2 cases and made an uneventful recovery.

The authors recommend that cases of acute benzene hexachloride poisoning should be treated by immediately emptying the stomach, combating signs of central excitation, and controlling the convulsions with intravenous calcium thiosulphate. The administration of milk, castor oil, and paraffin-containing purgatives is contraindicated.

Anne Tothill

243. Mode of Action of Some Toxic Substances: with Special Reference to the Effects of Prolonged Exposure. [Ernestine Henry Lecture]

J. M. Barnes. British Medical Journal [Brit. med. J.] 2, 1097-1104, Oct. 28, 1961. Bibliography.

Radiology

RADIODIAGNOSIS

244. Comparison of Radioisotope Scanning with Cerebral Angiography and Air Studies in Brain Tumour Localization

J. G. McAffe and D. R. TAXDAL. Radiology [Radiology] 77, 207-222, Aug., 1961. 10 figs., 7 refs.

The technique of cerebral radioisotope scanning is carried out 24 to 48 hours after the intravenous injection of ¹³¹I-labelled serum albumin in a dose of $2.5 \,\mu c$, per lb. (5.5 μ c. per kg.) body weight up to a maximum of 500 μc. The administration of 0.5 ml. of Lugol's iodine orally 2 hours before prevents the uptake of free ¹³¹I by the thyroid gland. The scintiscanner used by the authors at Johns Hopkins Hospital, Baltimore, is only briefly described. With the patient recumbent on an x-ray table the detector moves at 5 to 6 inches (12.7 to 15.2 cm.) per minute, advancing $\frac{3}{16}$ inch (4.7 mm.) at the end of each line so that each projection takes 25 to 30 minutes. Normally scans are made in the lateral, anterior, and posterior projections, the results being shown photographically on x-ray film. The brain contains a low concentration of isotope and shows as a pale area in the centre of the film surrounded by a darker zone due to isotope in the scalp, muscles, and blood vessels. Tumours and other space-occupying lesions are dark, as the breakdown of the blood-brain barrier around the tumour bed allows the labelled protein to permeate.

The authors have applied this technique in the investigation of 400 patients with suspected localized intracranial lesions. Of these patients, 71 were proved to have brain tumours, 52 of which were shown on scanning. This is an accuracy of 73% compared with an accuracy of 70% for cerebral angiography, which was carried out in 43 of the positive cases. Meningiomata, metastases, and glioblastomata were most easily detected, while cystic lesions, pituitary tumours, aneurysms, haematomata, and posterior-fossa lesions were rarely shown. Positive scans were obtained with 16 patients who did not have brain tumours, but most of these had other localized lesions such as encephalomalacia or arteriovenous fistula. Paget's disease was responsible for one false positive result. D. E. Fletcher

245. Cerebral Angiostratigraphy: First Practical Results

P. ROCCA and G. ROSADINI. Radiology [Radiology] 77, 223-227, Aug., 1961. 8 figs., 1 ref.

Cerebral angiostratigraphy by a technic permitting simultaneous demonstration of the intracranial vascular system at different levels has proved of value in clinical use. Dissociation of the vascular structures, layer by layer, makes possible determination of their volume and estimations of their depth.

Two cases are reported. In one, standard angiography showed a calcareous mass in the temporal region, on which some branches of the arteries of the sylvian group were projected. By angiostratigraphy it was possible to exclude a calcified abscess and to diagnose an oligodendroglioma with a central noncalcified nucleus and a calcific capsule, into which the vessels of the sylvian group entered. The diagnosis was confirmed surgically. The second patient had a parieto-occipital angioma. In this instance it was possible to demonstrate also a deep saccular dilatation which on the standard angiogram was obscured by overlying shadows.

It is believed that cerebral angiostratigraphy represents a diagnostic contribution of value, particularly in neuro-surgical cases, when it can furnish useful information to the surgeon.—[Authors' summary.]

246. The Roentgenologic Features of Acromegaly E. K. LANG and W. T. BESSLER. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 321-328, Aug., 1961. 4 figs., 24 refs.

The radiological features in 31 cases of acromegaly were studied by the authors at the Johns Hopkins Hospital, Baltimore. The disease is caused by hyperfunction of the anterior lobe of the pituitary gland with excessive production of growth hormone. Before epiphysial closure this results in gigantism, but thereafter in acromegaly. Radiological characteristics tend to develop rather late, but they support the clinical findings and are of some value in assessing the effect of treatment. Enlargement of the sella turcica, a purely local effect due to pituitary hyperplasia and varying greatly in degree, was the most common single feature, being seen in 29 of the 31 cases. The remainder of the changes observed are attributable to the action of the growth hormone.

Increased growth of appositional bone accentuates muscle and ligamentous attachments, being particularly evident in ungual tufts, tuberosities, and the occipital protruberance. Periosteal bone production causes such changes as an increase in the antero-posterior diameter of vertebral bodies, especially in the thoracic region, while overgrowth of the facial bones and elongation of the mandible produces the typical facies. Minimal endochondral growth in the deep layers of the articular cartilage may result in slight elongation of the long bones, even after the epiphyses have fused. Cartilage proliferation is stimulated. As a consequence the costo-chondral junctions enlarge to produce the "acromegalic rosary" while overgrowth of articular cartilage widens the joint spaces and, in the hands and less commonly the feet. contributes to elongation of the digits; similarly, the intervertebral spaces may show increased height. Such cartilage, however, is suspect in quality, since degenerative osteoarthritis, seen in 15 out of 20 cases, was earlier in onset than in non-acromegalics. The observation of uneven and irregular spur formation and absence of sclerosis of the vertebral end-plates led the authors to believe that radiological differentiation of this type of osteoarthritis could be made. Generalized and localized osteoporosis is another well-known feature. The sinuses enlarge from central resorption of bone and peripheral appositions, this being particularly marked in the frontal sinuses. The small bones of the hands and feet may be unduly slender from over-modelling, and the cranial vault may be abnormally thin, but sometimes bone apposition may result in the appearance of hyperostosis frontalis interna.

Treatment rarely caused regression of the osseous changes, except for recalcification of the clinoid processes and sella turcica.

R. O. Murray

247. The Occipito-atlanto-axial Joints in Rheumatoid Arthritis and Ankylosing Spondylitis

W. MARTEL. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 223-240, Aug., 1961. 16 figs., 45 refs.

Neck pain and stiffness are not uncommon in rheumatoid disease—a term here used to include not only rheumatoid arthritis and ankylosing spondylitis, but also the so-called rheumatoid variants. This paper from the University of Michigan, Ann Arbor, reports the results of radiological examination of the cervical spine in 66 adult patients, which was undertaken in view of the frequency of subluxation of the peripheral joints in the conditions mentioned above. The series consisted of 34 patients with rheumatoid arthritis and 32 with ankylosing spondylitis, all selected because of persistent neck discomfort or severe progressive disease. Plain lateral radiographs in flexion and extension were taken and, when necessary, supplemented by other views including lateral mid-line tomograms.

Abnormal atlanto-odontoid separation was demonstrated in 24 of the rheumatoid patients, in 11 cases the distance between these structures being greater than 5 mm.. compared with the upper limit of normal of 2.5 mm. In 12 of these patients erosion of the odontoid process was present and is considered to be more responsible for the subluxation than laxity of the transverse ligament of the axis. Such changes were less severe in the patients with ankylosing spondylitis, being seen in only 5 cases, but in 7 patients in this group there was an already established bony fusion between the odontoid process and the anterior arch of the atlas or the basilar process of the occiput. The great majority of these subluxations were demonstrable only in the position of flexion. Odontoid erosions were seen in 4 cases and reactive sclerosis ("shining odontoid") in another 4. Attrition of the bony structures produced pseudobasilar invagination in 10 of the rheumatoid and 9 of the ankylosing spondylitis group. Other cervical subluxations were also seen in both groups.

The author comments on the perplexing lack of significant neurological manifestations in this series and suggests that this may possibly be explained by the slow development of the lesions, which allowed adaptation of the spinal cord, and by the frequent reduction in size by erosion of the odontoid process. Nevertheless, neurological manifestations, sometimes severe, have been reported and the author suggests that their presence may be masked during examination by other deformities caused by the disease. Virtually all these patients had received steroid therapy, but further investigation is required before a correlation with this treatment can be established, as such lesions have certainly occurred in patients not given steroid therapy. It is concluded that these lesions are potentially dangerous, are more frequent than has been thought to be the case, and are often overlooked.

R. O. Murray

248. Destructive Lesions of the Vertebral Bodies in Rheumatoid Disease

W. B. SEAMAN and J. WELLS. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 241-250, Aug., 1961. 8 figs., 20 refs.

The authors report from Columbia University, New York, an investigation into the occurrence of destructive lesions of the vertebral bodies in rheumatoid disease. Such changes were found in 11 out of 110 patients with Marie-Strümpell arthritis and in 2 further patients with peripheral rheumatoid arthritis. A destructive focus in the upper or lower anterior corner of a vertebral body is first seen, involvement of the thoracic and lumbar spines being approximately equally frequent. Varying degrees of reactive sclerosis may be observed. In some cases the lesion remains localized and may even produce a sharpening of the vertebral corner, causing the vertebral body to become square in shape; some authors have considered this to be the origin of the square vertebral shape seen so commonly in ankylosing spondylitis. In other cases the destruction extends to involve the articular surfaces, when the appearance then closely simulates the changes found in chronic bacterial infections of the spine, but the lesions progress even more slowly than those of tuberculous infection. Narrowing of the affected disk is less common, occurs later, and produces no shadows such as those caused by paravertebral abscess. Although vertebral fusion may eventually occur with healing, the lesions rarely progress in the manner of those of infective origin.

In the discussion the authors note that steroid therapy cannot be the sole cause of these destructive phenomena, since 5-of the patients did not receive this type of treatment. While some of the most severe cases had in fact been given steroids, the continuation of treatment with these drugs did not necessarily result in further radiological deterioration. An unusual complication incidentally observed in the series was erosion of the odontoid and anterior arch of the atlas in one patient; marked subluxation of the atlanto-axial joint later developed but, despite severe neck pain, no clinical evidence of cord compression was found. Similar changes of this unusual type in 2 other patients are mentioned. [These incidental findings should be compared with those reported by Martel (see Abstract 247).]

R. O. Murray

249. Osteolysis of the Acromial End of the Clavicles in Rheumatoid Arthritis

M. ALFERT and M. MEYERS. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 251–259, Aug., 1961. 5 figs., bibliography.

Destructive changes affecting the outer ends of the clavicles in patients with advanced rheumatoid arthritis, have received little attention in the literature. In this report from the Presbyterian Hospital, New York, 11 such cases are described. Widespread clinical and radiological joint involvement had been established. Tapering of the outer ends of both clavicles was seen in 7 patients, in one of whom slow progression of the changes over 12 years is illustrated. The other 4 cases showed cortical erosion and pseudocyst formation, the acromic-clavicular joint spaces becoming widened as bone absorption took place. The normal angle formed by the acromic-clavicular joint with the sagittal plane was decreased.

The differential diagnosis is extensively discussed [but in view of the numerous changes caused by the disease elsewhere in the skeleton of these patients this must be somewhat academic]. The authors consider the clavicular erosions to be comparable to the loss of bone seen in other sites in arthritis mutilans.

R. O. Murray

250. Roentgen Changes in Reiter's Syndrome

W. V. Weldon and R. Scalettar. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 344-350, Aug., 1961. 9 figs., 10 refs.

This paper from the Walter Reed General Hospital, Washington, D.C., describes the radiological findings in 46 cases of Reiter's syndrome. Clinically, this syndrome consists essentially of non-specific urethritis and arthritis, with the classic conjunctivitis forming an inconstant member of the triad, while additional and not uncommon features are diarrhoea and muco-cutaneous lesions. The aetiology is unknown, but males are almost exclusively affected.

Polyarthritis is commonest in the lower limbs and sacro-iliac joints, and in the early stages radiographs are likely to show periarticular swellings and subchondral bone resorption. More severe changes may be expected when the illness lasts for several months or when attacks, as often happens, are repeated. Changes seen by the authors were as follows. (1) Para-articular joint erosions, affecting particularly the metatarso-phalangeal. and sacro-iliac joints. (2) Periosteal reactions were commonly seen along the shafts of the metatarsals and phalanges, and less often involved the bones of the hands. (3) New bone formation at the attachments of tendons and ligaments was a prominent feature. When this occurs at the attachments of the Achilles tendon or the plantar fascia on the calcaneus, resulting in the formation of spurs, with hazy and irregular margins, the authors consider the appearance to be virtually pathognomonic, assisting greatly in the otherwise difficult differentiation of the syndrome from early rheumatoid arthritis.

The initial changes are reversible when the disease subsides, but lesions of the sacro-iliac joints are likely to be progressive. In Reiter's syndrome, unlike ankylosing spondylitis, spinal involvement is rare; it was seen in only one case in this series, when minimal bridging between vertebral bodies was observed. The findings confirm previous reports on the subject and emphasize a specific feature of the disease to be a fluffy, prolific, periosteal reaction on the plantar surface of the calcaneus.

R. O. Murray

251. Accuracy of X-ray Diagnosis of Ulcerative Gastric Lesions

G. N. STEIN, F. F. PAUSTIAN, A. K. FINKELSTEIN, and M. GOLDMAN. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 148-159, Aug., 1961. 2 figs., 30 refs.

At the Graduate Hospital of the University of Pennsylvania the accuracy of radiological diagnosis was. studied in 129 patients with gastric ulcer under the care of a single gastroenterologist. [No clinical details are given, the proportions of ulcers in the upper, middle, and lower thirds of the stomach are not stated, and there is no mention of associated duodenal or pyloric ulcers or scars.] The ulcers were classified by the radiologist as (1) definitely benign, (2) definitely malignant, (3) probably benign, (4) probably malignant, or (5) indeterminate and this classification is recommended for universal use Ithough the statistical evidence leaves it doubtful whether anything is gained by separating the last 3 groups]. The final diagnosis was made either by histological examination or by the response to medical treatment, healing of the crater and a lack of recurrence on 5-year follow-up being regarded as evidence of benignity; failure to respond to medical treatment for 10 to 14 days in a case in which the radiological diagnosis had been "benign" led to its transfer to the "probably malignant" group.

The results were as follows:

X-ray, diagnosis	No. of Cases	Final Diagnosis		Accuracy
		Benign	Malignant	of X-ray Diagnosis
Definite diagnosis Benign Malignant	73 28	- 71 - 0.	2 28	97·2% 100%
Total	101	-71	. 30 .	- 98%
Probable diagnosis Benign Malignant	16 6	11 3	5 3	68·8% 50%-
Total	22	14	- 8	63.6%
Indeterminate	6	· 2	4 ,	,

From an analysis of the x-ray findings in these cases the only criteria which proved "reasonably trustworthy" for making a radiological diagnosis were the character of the neighbouring mucosal folds, the contour of the filling defect above and below a true profile view of the ulcer, and the presence of a thin radiotranslucent line across the neck of the ulcer crater in profile compression films [referred to in this paper as "Hampton's line"]. Other criteria for distinguishing between simple and

malignant craters proved unreliable and it is recommended that they should be abandoned.

[It is unfortunate that there is no discussion of the site of the ulcers. There is generally no excuse for taking a risk in the case of an ulcer in the lower half of the stomach in a young patient, whereas it is justifiable to take a considerable risk with a high ulcer just below the cardia in an elderly patient, especially as a carcinomatous ulcer at this site is unlikely to be curable.]

Denys Jennings

252. Duodenal Ulcer: Clinical and Radiological Evaluation of Intractability

J. H. DAVIDSON and J. G. TEPLICK. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 171-175, Aug., 1961. 3 figs., 3 refs.

Posterior penetration of a duodenal ulcer is common and seems to make it intractable to medical management. Even in the absence of a demonstrable crater, changes in the descending duodenal loop often suggest the diagnosis. These changes are defined by the authors as follows. (a) Loss of normal valvulae conniventes or serrations on the inner aspect of the loop; the absence must be consistent in serial films. (b) Stiffening of the same area. (c) Occasional posterolateral displacement of the loop. (d) Coarsening of the mucosal folds. This last sign is less frequently seen.

In 30 cases in which these loop changes were observed at the Kensington Hospital, Philadelphia, the diagnosis of posterior penetration was confirmed surgically. Three recent examples are described in detail in this paper.

[No information is given about how frequently posterior penetration is diagnosed radiologically or how often it has been incorrectly diagnosed. In Great Britain possibly too much stress is laid on the diagnosis of an ulcer and too little on the radiological assessment of the extent of the structural damage.]

Denvs Jennings

253. The Roentgenographic Findings in Cases of Gastric Biliary Calculi

N. B. LONGLEY and A. R. MARGULIS. Surgery [Surgery] 49, 719-722, June, 1961. 3 figs., 12 refs.

254. X-ray Diagnosis of Hiatus Hernia. (Röntgendiagnose der Hiatushernie)

E. HAFTER. *Radiologe* [*Radiologe*] 1, 141-147, Aug., 1961. 11 figs., 16 refs.

The author considers that hiatus hernia is frequent, since among 2,200 private patients with upper abdominal pain he found an incidence of 16.5%, compared with one of 18.1% for gall-stones, 14.3% for duodenal ulcer, and 5.4% for gastric tumour; the incidence rises with advancing age. For radiological demonstration of the hernia the author uses a thick barium paste which the patient takes from a feeding cup; the importance of having the stomach well filled by the barium is stressed. He recommends the horizontal position, the patient lying supine turned towards the left with the head lowered. It also helps if the intra-abdominal pressure is increased. In the fat patient this can be done by having the patient

prone, while in the thin patient he applies non-opaque pads to increase the pressure. It is considered important to take exposures in expiration to avoid diagnosing the phrenic ampulla as hiatus hernia.

It is not always easy to recognize where the oesophageal mucosa ends and the gastric mucosa begins, but the following points are considered important. The lowermost part of the oesophagus, that usually below diaphragmatic level, behaves differently from the rest of the oesophagus, because it is normally narrower than the rest of the oesophagus. Sometimes when herniated it, forms a contracted area about 1 inch (2.5 cm.) long. On the other hand this particular segment is capable of considerable ballooning. When this takes place three contraction rings become recognizable, the uppermost ring corresponding to the junction of that part of the oesophagus normally above the diaphragm and the part normally below the diaphragm. This uppermost ring is inconstant and results from muscular contraction. The lowermost ring appears when the hiatus contracts on full inspiration; it disappears on expiration and the barium then flows towards the stomach. In about half the cases a third ring may be seen between the two previously mentioned rings. This ring, which is inconstant in diameter and width; represents the border between the' oesophageal and gastric mucosa. It seems to be caused by the presence of more fibrous tissue in that area which resists expansion. If on inspiration a hernia-like structure appears, no greater than 3 cm. in length, and if its outline is smooth this can only be the ampulla. If the structure is greater than 3 cm. and shows a ring-shaped contraction in the middle it must be a hiatus hernia with the expanded ampulla resting cap-like on its top. Only those cases in which actual gastric mucosa is found above diaphragmatic level can be rightfully classified as hiatus hernia.

In conclusion the author recalls that a true hiatus hernia may appear to lie below the dome of the diaphragm in oblique projections, since the part of the diaphragm where the hiatus is situated lies so much lower than the dome. This fact has been stressed before but seems to have been largely forgotten.

F. M. Abeles

255. Omental Diaphragmatic Hernia and Partial Right Diaphragmatic Relaxation with Humped Liver. (Über diaphragmale Netzhernien und partielle Relaxionen der rechten Zwechfellhälfte mit Leberbuckel)

G. LINDEN. *Radiologe* [*Radiologe*] 1, 157-161, Aug., 1961. 6 figs., 7 refs.

The author points out that large upward bulges of the anterior part of the right diaphragm are frequently seen and are often the result of a partial relaxation of the diaphragm. As a consequence the liver, which has a great degree of plasticity, forms large upward bulgeseither in true hernia or in partial relaxation. True parasternal hernia exists and is probably more frequent on the right side. On the left side the heart seems to exercise a protective function. In true hernia the omentum may be herniated and this can be demonstrated with the aid of pneumoperitoneum, provided there are no adhesions due to inflammation.

F. M. Abeles

256. On Coronary Arteriography: Findings in the Coronary Arteries on Selective Aortic and Left-sided Cardiography in Congenital and Acquired Heart Disease (Zur Koronarographie: Koronararterienbefunde im selektiven Aorto- und Laevokardiogramm bei/angeborenen und erworbenen Herzsehlern)

A. DÜX, H. H. HILGER, A. SCHAEDE, and P. THURN. Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmidizin [Fortschr. Röntgenstr.] 95, 1-23, July, 1961. 18 figs., bibliography.

In this discussion of coronary arteriography, presented from the University of Bonn, the authors point out that although generally speaking a normal arrangement of the coronary arteries is met with in most cases, anatomical variations do occur. Thus sometimes there is a prevalence of the left and sometimes of the right coronary artery, while other anomalies are the origin of one coronary artery from the pulmonary artery, or the left coronary artery may arise from the right, or vice versa. The myocardial venous system also has its variations. Small venous occur occasionally in the myocardium and open into the cardiac space, the so-called veins of Thebesius or venae cordis minimae.

Mostly the coronary arteries are well visualized on aortography after the injection of 50 ml. of 76% "urografin" (diatrizoic acid). In selective left cardiography, however, the filling of the coronary arteries is not equally reliable, and here left lateral films are generally the most satisfactory. An impression of prevalence of either the left or the right coronary artery should be judged with some reservation, since hypertrophy of one of the chambers of the heart must of course influence the flow through either of the vessels. The authors are of the opinion If that the coronary arteries are wider and more strongly filled in systole, the reason being that they run outside the heart wall, as least as far as the main branches are concerned, and the stronger filling is caused by the back pressure stemming from the contracted finer branches, which run within the heart muscle. They suggest that this fact has to be borne in mind when the therapeutic effect of drugs is being assessed. F. M. Abeles

257. Impending Aortic Rupture: Pathogenesis of X-ray Signs

C. T. DOTTER, N. R. NILES, and I. STEINBERG. New England Journal of Medicine [New Engl. J. Med.] 265, 214–221, Aug. 3, 1961. 5 figs., 9 refs.

Aneurysms likely to rupture are characterized by a serious if not complete loss of muscular or elastic tissue, which is replaced by blocd clot, atheroma, and fibrous connective tissue. Small haemorrhages into the aortic wall, beginning in the intima and subsequently extending, are believed to play an important part in the development of arteriosclerotic lesions, and are probably the major cause of the medial destruction that results in aneurysm formation. The rate of aneurysmal dilatation varies with the size and extent of the initial haemorrhage, the extent of the destruction of medial smooth muscle and elastic tissue, the strength and distribution of reactive fibrous connective tissue at the outer surface of the aortic wall, and the intraluminal pressure. Radiologically, in

cases of impending rupture of the thoracic aorta there may be rapid enlargement of the aneurysm, loss of marginal sharpness, and development of adjacent pulmonary infiltrations due to leakage of blood. Pleural and pericardial effusions may also occur.

John H. L. Conway-Hughes

258. Cardioangiographic Studies of the Mitral and Aortic Valves. [Monograph, in English]
S. R. KJELLBERG, B. NORDENSTRÖM, U. RUDHE, V. O. BJÖRK, and G. MALMSTRÖM. Acta radiologica [Acta radiol. (Stockh.)] Suppl. 204, 1–85, 1961. 45 figs., bibliography.

259. Some Radiological Aspects of Scurvy in the Adult N. Joffe. British Journal of Radiology [Brit. J. Radiol.] 34, 429-437, July, 1961. 13 figs., 12 refs.

The literature, aetiology, and clinical aspects of scurvy are first briefly discussed in this paper from Baragwanath Hospital, Johannesburg. It is pointed out that occasional cases occur among the South African Bantu population as a result of prolonged cooking of the meat and vegetables in the diet, with consequent destruction of the only available source of vitamin C. The radiological findings in 39 adults known to be scorbutic are then described. The series originally included 53 adults, but in order to avoid confusion with post-menopausal and senile osteoporosis all females and all patients over 55 were excluded.

In 18 of the 39 patients the radiographs were normal, in spite of the presence of advanced clinical signs of scurvy. In the remainder spinal osteoporosis was common and in 13 cases vertebral bodies had undergone compression fractures, often in the absence of a history of significant trauma. These changes varied from simple biconvexity to wedging and complete vertebral flattening. Diffuse osteoporosis of the bones of the legs was also common. This was accentuated and mottled in type round the knees or ankles where movement had been restricted by the development of haemarthrosis or haemorrhage into surrounding soft tissues. Such phenomena were attributed to disuse. Uniform periosteal reactions on the shafts of long bones, with or without generalized osteoporosis, were also seen; although of uncertain cause, they were considered likely to result from periosteal irritation by haemorrhages. None of the adults. however, showed the large subperiosteal hacmatomata commonly found in scorbutic children, although one example of this is reported from the literature.

Haemarthroses equally affected knees and ankles; the hips were exempt. The appearance of affected joints differed in no way initially from synovial effusions and intra-articular haemorrhages of other origin, but in severe cases gross soft-tissue swelling and intense para-articular osteoporosis was accompanied by some destruction of the bony articular surfaces.

The changes described correspond with theoretical expectations in adult scurvy, being essentially due to osteoporosis and capillary fragility. They do not support the "generally expressed view that radiological abnormalities are not, as a rule, observed in cases of scurvy in the adult".

R. O. Murray

ABSTRACTS OF WORLD MEDICINE

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Pathology

260. Progressive Systemic Sclerosis and Malignant Hypertension: Immunohistochemical Study of Renal Lesions

R. H. FENNELL JR., C. R. R. M. REDDY, and J. J. VAZQUEZ. Archives of Pathology [Arch. Path.] 72, 209-215, Aug., 1961. 8 figs., 12 refs.

The authors, working at the School of Medicine and Presbyterian Hospital, Pittsburgh, studied the localization of fibrinogen and/or fibrin, albumin, and γ globulin in the renal lesions of 3 patients with progressive systemic sclerosis (scleroderma) and 3 with malignant hypertension by the immunofluorescent technique.

The lesions in both groups were similar. The areas of mucoid intimal thickening of the small arteries and fibrinoid necrosis of the arterioles and glomeruli stained with the antifibrinogen serum, indicating the presence of material antigenically like fibrinogen, but contained little albumin or y globulin. When the serum of one patient with scleroderma was conjugated with fluorescein isothiocyanate, staining of nuclei was observed, indicating the presence of antinuclear antibody. Sera from the other patients with scleroderma gave inconstant staining, while those from the patients with malignant hypertension gave negative results.

The authors conclude that the similarity of the renal lesions in these two conditions might reflect a common pathogenesis despite the differing actiology of the basic disease process.

G. L. Asherson

EXPERIMENTAL PATHOLOGY

261. Endogenous Factors Responsible for Leucocytic Emigration In vivo

J. V. HURLEY and W. G. SPECTOR. Journal of Pathology, and Bacteriology [J. Path. Bact.] 82, 403-420, 1961. 11 figs., 17 refs.

This paper from University College Hospital Medical School, London, describes experiments on rats and rabbits designed to investigate the role of endogenous substances in causing emigration of leucocytes following tissue injury, produced in this study by exposure to heat at 55° C. for 30 seconds. Observations of leucocyte emigration were first made on sections of rat skin removed 40 minutes after the intradermal injection of 0.1 ml. of extracts prepared from the animal's skin and subcutaneous tissue obtained at 1, 5, and 20 hours after the thermal injury. Whereas the extracts of skin obtained at 1 hour after injury possessed only slight activity, those of tissue ob-

tained at 5 and 20 hours were highly effective in producing leucocyte emigration, large numbers of the cells being seen passing through the walls of the capillaries and small venules in the injected area. The view that the contained leucocytes in the burned skin were the effective agents was supported by the finding that extracts of rat polymorphonuclear leucocytes obtained from peritoneal exudates and from blood were also effective.

In the experiments on rabbits peritoneal exudates obtained from animals previously depleted of polymorphonuclear leucocytes by treatment with nitrogen mustard were shown to contain insignificant numbers of these cells, but were nevertheless found to be active in inducing leucocyte emigration. Likewise, extracts of rat skin burned 5 hours previously were equally effective in rats which had been treated with nitrogen mustard, although sections from the burned tissue revealed a total absence of polymorphs. An extract of serum alone and one of liver alone were inactive, but when serum and liver were incubated together it was possible to obtain an extract which was highly effective in producing leucocyte emigration.

These results suggest that some factor in the serum is activated by damaged tissue or polymorphs and so becomes capable of producing leucocytic emigration. It was shown that this substance is non-dialysable, heat labile, and destroyed by trypsin, indicating that it is a protein, possibly an enzyme. The authors conclude there may be an endogenous system responsible for leucocyte emigration comprising a serum precursor, an activator present in certain tissues, and the active principle itself. It is suggested that following injury, damaged tissue cells or polymorphs activate the serum factor to induce leucocyte emigration.

Hewett A. Ellis

262. Delayed Leucocytić Emigration after Intradermal Injections and Thermal Injury

J. V. Hurley and W. G. Spector. Journal of Pathology and Bacteriology [J. Path. Bact.] 82, 421-429, 1961. 8 figs., 10 refs.

In this further communication [see Abstract 261] the authors describe the delayed leucocytic emigration which occurs in response to thermal injury and to the intradermal injection of histamine (which increases capillary permeability), saline solution, and homologous serum. The injected or damaged tissue was prepared for histological study by methods described, and examined at various intervals of time after the injection or thermal injury. Comparison between tissues obtained 1, 2, 4, 6,

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18, and 22 hours after the injection of histamine (100 μ g. per ml.) and saline revealed certain differences in the histological appearances. Thus after histamine there - was considerable oedema up to 8 hours, whereas no oedema occurred after injections of saline. The injections of both substances, however, produced dilatation of the vessels, margination of leucocytes, and a delay in the local emigration of leucocytes, the latter not reaching its maximum until 4 to 6 hours later. Injections of homologous serum produced comparable changes, although in this case leucocyte emigration tended to occur over a wider area and there was less oedema than that produced by histamine. Parallel studies of the changes in capillary permeability (as indicated by the degree of leakage into the affected area of the dye trypan blue given intravenously) which followed the injection of histamine revealed that the increase in capillary permeability bore no relation in time to the onset of leucocytic emigration. A similar dissociation of changes in capillary permeability and leucocytic emigration was observed following thermal burns in tissue studied at regular intervals after injury:

Since the onset of leucocytic emigration is delayed and occurs some hours after the effects of the injected saline or histamine have disappeared it is considered unlikely that such emigration is brought about by the direct action of these substances on the vessel walls. It is possible that there is some endogenous mechanism responsible for the emigration of polymorphonuclear leucocytes and that this requires a certain time to come into effect. The existence of such an endogenous mechanism would explain the similarity in the time relations of the responses obtained with the various substances tested. It is concluded that the clear dissociation between the increased capillary permeability and leucocytic emigration strongly indicates that these are distinct phenomena. The authors add that if the results of recent work by various workers cited, which suggests that fluid and protein escape through the cytoplasm of the endothelial cells themselves whereas leucocyte emigration probably occurs between the endothelial cells, are confirmed "the evidence of separation of the two elements of the acute inflammatory response would be almost complete". Hewett A. Ellis

263. Experimental Ulcerative Colitis Produced by Anticolon Sera

H. H. LEVEEN, G. FALK, and B. SCHATMAN. Annals of Surgery [Ann. Surg.] 154, 275-280, Aug., 1961. 8 figs., 13 refs.

The authors, working at the Veterans Administration Hospital, Brooklyn, New York, produced antibodies in rabbits and ducks by the injection of dog colon. The injection of the antiserum into dogs was followed within a few hours by the passage of loose, watery motions lasting up to one month, with sometimes further bouts of diarrhoea after a period of normal stools. In some cases histological examination showed ulceration of the colon with variable loss of mucosa and infiltration with inflammatory cells. In 4 of the 6 dogs injected antibody against erythrocytes coated with colon extract from adult rabbits was found at a time when the injected rabbit

serum would presumably have been eliminated. No significant changes were found in guinea-pigs injected with antibody to guinea-pig colon. The authors conclude that antibodies against dog colon damaged normal dog colon and stimulated the production of antibody against a component of dog-colon homogenate.

G. L. Asherson

CHEMICAL PATHOLOGY

264. The Calcium Fractions of Plasma in Hypercalcaemic Conditions and in Adult Coeliac Disease D. I. FOWLER, D. J. FONE, and W. T. COOKE. *Lancet* [Lancet] 2, 284–287, Aug. 5, 1961. 4 figs., 19 refs.

In an investigation carried out at the General Hospital, Birmingham, using ethylenediamine tetraacetic acid for titration and murexide as indicator it was found that the mean plasma total calcium level in 35 healthy adults was 9.84 mg. (range 9.32 to 10.36 mg.) per 100 ml. In 20 of these subjects the mean diffusible calcium value (determined by ultrafiltration) was 6-04 mg. per 100 ml., while in 11 of them the mean ionized calcium value (by Rose's method) was 5.85 mg. per 100 ml. and the complexed calcium value 0.27 mg. per 100 ml. It is noted that the levels of plasma diffusible calcium and ionized calcium were both raised in 9 patients with hypercalcaemia of varied origin; determination of these values is therefore of no value in the differential diagnosis of hypercalcaemia. Of 25 patients with adult coeliac disease, the plasma total calcium level was reduced in 15, the other fractions usually also being reduced, except that for complexed calcium, which was raised. The lowest values for ionized and diffusible calcium were found in patients with active osteomalacia.

M. Lubran

265. Simple Test-paper Method for the Clinical Determination of Plasma Pseudocholinesterase

H. C. CHURCHILL-DAVIDSON and W. J. GRIFFITHS. British Medical Journal [Brit. med. J.:] 2, 994–995, Oct. 14, 1961. 1 fig., 9 refs.

A test-paper containing acetylcholine and bromothymol blue was used at St. Thomas's Hospital, London, as a simple method of grading the level of plasma pseudocholinesterase. When plasma is applied to the paper the liberation of acid, because of the hydrolysis of acetylcholine, results in a change of colour. The time when a particular colour is obtained gives an indication of the level of plasma pseudocholinesterase activity. It is suggested that the method may be useful in detecting low levels of plasma pseudocholinesterase in patients about to undergo anaesthesia with the use of suxamethonium as a muscle relaxant.

H. Harris

266. Tubeless Gastric Analysis with Azure A and Betazole Hydrochloride

O. A. A. Bock and L. J. Witts. *British Medical Journal* [*Brit. med. J.*] **2**, 665–667, Sept. 9, 1961. 37 refs.

Using 50 mg. of the histamine isomer betazole hydrochloride ("histalog") as the stimulant for acid production in the "tubeless gastric analysis" test performed

with azure A, the authors obtained positive results in 66 search, Sydney. The procedures, which require 0.5 ml. of 105 patients examined at the Radcliffe Infirmary, Oxford. Acid secretion was confirmed by means of an augmented histamine test in 27 out of 29 of the patients' who had shown a positive result in the tubeless test; the remaining 2 patients with a false positive result gave a negative result with the tubèless test when it was repeated. Achlorhydria was confirmed by the augmented histamine test in 18 of 21 patients tested in whom the tubeless test had given a negative result. When 500 mg. of caffeine benzoate was used as the gastric stimulant in the azure A test in 77 patients the result was positive in 51 and negative in 26. Of 17 of these negative cases, achlorhydria was confirmed by the augmented histamine test in 11.

The authors conclude that the tubeless test using azure A as indicator and betazole hydrochloride as stimulant appears to be a satisfactory screening test for achlorhydria. M. Lubran

267. Studies on the Disturbance of Glucuronide Formation in Infectious Hepatitis

M. F. VEST and E. FRITZ .- Journal of Clinical Pathology [J. clin. Path.] 14, 482-487, Sept., 1961. 4 figs., 18 refs.

The ability of the liver to form glucuronides was measured in 10 children with infective hepatitis at the Children's Hospital of the University of Basle. One test was performed at the onset and another about 4 weeks later, after the clinical symptoms had disappeared. N-acetyl-p-aminophenol (N.A.P.A.) was injected intravenously in a dosage of 10 to 20 mg. per kg. body weight into 6 of the children and acetanilide, which is rapidly oxidized to N.A.P.A., was given by mouth in a similar dosage to 4. N.A.P.A. is conjugated by the liver at the hydroxyl group and excreted in the urine as sulphuric and glucuronic acid conjugates. Total conjugated p-aminophenol, free N.A.P.A., and N.A.P.A. glucuronide were measured in 24-hour collections of urine and in blood samples collected at intervals up to 9 hours after administration.

During the acute phase of hepatitis the excretion of total conjugated p-aminophenol and of N.A.P.A. glucuronide in the urine was about 20% lower than that after recovery from the disease; likewise free N.A.P.A. disappeared more slowly from the circulation and the peak concentration of N.A.P.A. glucuronide in the serum was lower (1.6 to $10.2 \mu g$. per ml.) at the onset of hepatitis than after clinical cure (3.9 to $17.2 \mu g$. per ml.). These results show that, as with other transformation mechanisms, glucuronide formation is depressed during the acute stage of infective hepatitis. J. E. Page

268. Rapid Incremental Methods for the Determination of Serum Iron and Iron-binding Capacity

R. N. BEALE, J. O. BOSTROM, and R. F. TAYLOR. Journal of Clinical Pathology [J. clin. Path.] 14, 488-495, Sept., 1961. 15 refs.

The reliability of colorimetric methods for the determination of the transferrin iron content and the latent iron-binding capacity of blood serum has been studied at the Institute of Clinical Pathology and Medical Reof serum if bathophenanthroline or its sulphonate is used or 1.0 ml, if o-phenanthroline is used as complexing agent, are described in detail. The authors conclude that these methods are suitable for routine clinical use; 3 or 4 serum samples may be analysed in 30 minutes. The results of measurements on sera from 12 normal males and 14 females are reported and compared with the results reported by other workers using other methods. In view of certain discrepancies between these figures it is suggested that a comparative study of the various methods J. E. Page . is needed.

269. Seromucoid in the Diagnosis of Cancer

E. CAMERON, A. CAMPBELL, and W. PLENDERLEITH. Scottlsh Medical Journal [Scot. med. J.] 6, 301-307, July, 1961. 14 refs.

Seromucoid estimations have been carried out by a slight modification of the method of Winzler et al. (J. clin. Invest., 1948, 27, 609; Abstr. Wld Med., 1949, 5; 552) on over 1,000 patients at the Royal Alexandra Infirmary, Paisley, Renfrewshire. The results are now reviewed with particular reference to the potential value of." the test in the diagnosis of cancer. The association of high seromucoid levels with malignant diseases has been confirmed. The significance of this rise in seromucoid level, its relationship to individual tumour pathology. and the interpretation of results are discussed. Although the test is not specific for neoplasia, it is believed that the information it provides can often be of great diagnostic and prognostic value. L. A. Elson

270. Seromucoid in the Diagnosis of Jaundice

E. CAMERON, A. CAMPBELL, and W. PLENDERLEITH. Scottish Medical Journal [Scot. med. J.] 6, 308-310, July, 1961. 3 refs.

From estimations in 73 cases at the Royal Alexandra Infirmary, Paisley, Renfrewshire, it has been found that patients with hepato-cellular jaundice have seromucoid levels below the normal range, while those with malignant biliary obstruction have levels significantly higher than normal. The levels in non-malignant biliary obstruction range from normal in non-infected cases to high values in patients with secondary cholangiitis.

The test is thus considered a valuable method of distinguishing hepato-cellular from obstructive jaundice, and its routine use is recommended in the diagnostic investigation of jaundiced patients. L. A. Elson

. 271. Evaluation of Radiolodinated Hippuran for the Estimation of Renal Plasma Flow

M. K. BURBANK, W. N. TAUXE, F. T. MAHER, and J. C. HUNT. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 36, 372-386, July 19, 1961. 3 figs., 17 refs.

Renal clearance studies were made on a series of 24 patients with hypertension or recently recovered from acute renal failure in which para-aminohippuric acid (PAH) and radioiodinated (131I) "hippuran" (sodium o-iodohippurate) were used simultaneously. The PAH values in 70 individual collection periods were, on the

average, significantly greater than the radioactive-hippuran clearances, the average clearance ratio hippuran being 0.87. Possible reasons for this difference are discussed, and it is suggested that the free-iodide content of the hippuran is significant. It is also suggested that pure radioactive hippuran will give results which are essentially the same as those obtained when PAH is utilized, and that the general procedure involved would be much simpler.

H. Harris

272. Clinical Use of Lactic Dehydrogenase R. J. ERICKSON and D. R. MORALES. New England Journal of Medicine [New Engl. J. Med.] 265, 478–482, Sept. 7, 1961, and 531–534, Sept. 14, 1961. Bibliography.

MORBID ANATOMY AND CYTOLOGY

273. Morphology of Tuberculosis of the Spine. (Морфологическая характеристика туберкулева поввоночника)

V. A. TALANTOV. Apxus Патологии [Arh. Patol.] 23, 25-31, No. 9, 1961. 7 figs., 24 refs.

The author presents the results of the pathologicoanatomical examination of surgical and necropsy specimens removed from 106 cases of tuberculosis of the spine. In 54 of these patients the onset had been in childhood, but in the remaining 52 after the age of 15. The disease was observed to be in it's early stages in 19 of the children and 21 adults; in both groups multiple foci were present, these being situated as a rule in the peripheral portions of the vertebral bodies. In children with duration of the disease of a year or more there was already extensive destruction of the vertebral bodies, with in some cases complete disintegration of several vertebrae and the intervertebral disks and formation of perifocal abscesses, while fistulae were present in almost all children in whom the disease had been present for over 2 years. In adults the progress of the disease was slower and both the destructive and reparative processes were less marked than in the children. A. Swan

274. Acute Porphyria: Necropsy Studies in Nine Cases F. W. Ten Eyck, W. J. Martin, and J. W. Kernohan. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 36, 409-422, Aug. 16, 1961. 2 figs., 13 refs.

This paper from the Mayo Clinic reports the necropsy appearances in 9 cases of acute porphyria, the diagnosis of which was made on the basis of biochemical and clinical findings. The patients were all males and ranged in age from 19 to 44 years. The brain was examined post mortem in 6 cases and peripheral nerves in all 9. The stains used for the histological studies are enumerated and the case history and an outline of the macroscopic and histological findings are given in each case.

Abdominal pain occurred in 5 patients and was the presenting symptom in 4. Neurological manifestations, ranging from motor weakness to flaccid paralysis, occurred in 4 cases. Visual disturbances, bulbar

involvement with respiratory palsy, and mental changes were each present in 3 cases. Although the fresh urine might be colourless, porphobilinogen, Waldenström's uroporphyrin, and increased quantities of coproporphyrin were found in most cases. All but one of the patients gave a history of exacerbations caused by barbiturates and in 3 cases the terminal illness followed the administration of a barbiturate, usually thiopentone for surgical anaesthesia. A family history was proved in one case and was likely in 2 others.

At necropsy in 7 of the cases emaciation and muscular atrophy were present and in 4 there was neurogenic muscular atrophy with hyaline degeneration. Pulmonary embolism with infarction occurred in 3 patients with weakness of the legs, and the advisability of administering anticoagulants in such cases is discussed. Histologically, iron-free, golden brown, lipochrome granules were seen in the liver cells in 5 cases and 8 patients had testicular atrophy with decreased or absent spermatogenesis. In all cases there were changes in the nervous system, namely, active focal degeneration of axis cylinders in zones of extensive demyelinization and Schwann-cell proliferation. Chromatolysis of dorsal root ganglion cells was present in 3 cases and anterior horn cell chromatolysis was found in all. Chromatolysis or shrinkage of the dorsal motor nuclei of the vagus and hypoglossal nerves was found in 3 out of 6 cases.

Other diseases, potentially fatal, were present in 7 of the 9 cases. It is suggested that in the absence of such complications symptomatic treatment, such as the use of anticoagulants, "may result in a decreased mortality rate".

F. Hillman

275. Occlusive Intrapulmonary Vascular Anomaly in the Newborn: a Cause of Congenital Pulmonary Hypertension?

E. Rubin and L. Strauss. American Journal of Pathology [Amer. J. Path.] 39, 145-161, Aug., 1961. 14 figs., 37 refs.

At the Mount Sinai Hospital, New York, the authors observed 5 newborn infants suffering from multiple congenital (including cardiac) anomalies whose intrapulmonary vasculature showed unusual changes. These changes were restricted to the small muscular arteries and occasionally the arterioles.

In the affected vessels a pronounced intimal proliferation was found with consequent reduction of the lumen. The endothelial lining could always be distinguished as a single layer of cells covering the intimal cushion. The cells forming the cushion were plump, with abundant clear cytoplasm and round nuclei resembling those of smooth muscle cells in the vascular media. Elastic and collagenous fibres were absent. The cellular proliferation was segmental and usually located in the initial segment of a small muscular artery. The arterial segments involved were either lacking an internal elastic membrane or the membrane was greatly attenuated or interrupted. The adventitia could be as much as twice the usual thickness and consisted mainly of collagenous fibres with a few elastic fibres admixed. The vessels of the systemic circulation appeared normal.

The authors state that the presence of congenital intrapulmonary vascular alterations may explain why in some instances even early surgical repair of cardiac anomalies may fail to prevent or correct pulmonary hypertension.

H. Caplan

- 276. Rheumatic Mitral Valve Disease in the Elderly: Incidence Found at Necropsy

T. HARGREAVES. British Medical Journal [Brit. med. J.] 2, 342-345, Aug. 5, 1961. 21 refs.

The incidence of mitral valve disease found at post-mortem examination in patients over the age of 50 is reviewed. In a 13-year period 2,086 necropsies were performed in patients over the age of 50. Of these, 64 (3.1%) had mitral valve disease: in 47 (73%) of them death was thought to be due directly to that condition. In 4 cases the presence of a mitral valve lesion was not suspected during life. The heart was enlarged in 62 (97%) cases. Gross dilatation of the left atrium was found in 6 cases and gross dilatation of the right atrium in one case. Active rheumatism was present in one case. Emboli were found in 13 (20%) cases at necropsy.

A history of rheumatic fever or chorea was found in 27 (42%) cases. Twelve of the 37 women had borne altogether 27 children. Shortness of breath on exertion was the presenting symptom in 34 (53%) cases. A middiastolic murmur was present in 30 (47%) cases. There was a record of auricular fibrillation at some period during life in 40 (63%) cases. A blood-pressure of greater than 150/90 was recorded in 22 (34%) cases.

The possible causes of longevity in mitral stenosis and the significance of the findings in relation to valvotomy and its prognosis are discussed.—[Author's summary.]

277. Light- and Electron-microscopic Study of Skin Capillaries of Diabetics

 AAGENAES and H. Moe. Diabetes [Diabetes] 10, 253-259, July-Aug., 1961: 4 figs., 19 refs.

A histological study of the skin and subcutis of 24 diabetic patients and 9 controls is reported from the Steno Memorial Hospital and the University, Copenhagen. The sections examined were stained with haematoxylin and eosin (van Gieson's method) and by the periodic-acid-Schiff (P.A.S.) technique.

The capillaries of the 9 non-diabetic subjects were essentially normal. In 12 patients in whom diabetes mellitus was detected before the age of 40 years there was a P.A.S.-positive thickening of the capillary walls, notably in the papillae of the dermis and around sweat glands. The changes were uneven, the same tissue section having almost normal and greatly thickened capillaries. Ectatic dilatations similar to micro-aneurysms were not seen, but the P.A.S.-positive material was frequently considerably more evident on one side than on the other side of a capillary. In 12 patients in whom diabetes was detected after the age of 40 years no or only slight capillary changes were found.

Pulp biopsy specimens from 2 healthy and 4 diabetic males, all aged about 30, were examined under the electron microscope. Most of the capillaries from the diabetic patients had far thicker walls than those of corres-

ponding capillaries from normal skin. The thickening was due primarily to periendothelial deposition of a material similar in density and structure to the basement membrane. The deposited material contained no collagenous fibrils, was usually compact and dense, and sometimes appeared stratified.

The similarity of these changes to those found in glomerular capillaries of diabetics is discussed. The authors consider that "the observations reported add support to the concept that diabetes mellitus is associated with a diffuse capillary vascular disease".

H. Caplan

278. Changes in Bronchial Epithelium in Relation to Cigarette Smoking and in Relation to Lung Cancer
O. AUERBACH, A. P. STOUT, E. C. HAMMOND, and L. GARFINKEL. New England Journal of Medicine [New Engl. J. Med.] 265, 253–267, Aug. 10, 1961. 5 refs.

The tracheobronchial tree has been dissected out and studied in 402 white males who have come to necropsy since 1954 at hospitals in and around New York. Included were all white males whose history indicated either that they had never smoked regularly or that they had smoked cigarettes regularly up to the time of their last illness; also all white males who had died of lung cancer irrespective of their smoking habits. Of the 63 patients in the last category, one was a 41-year-old man who had worked in an asbestos factory for 23 years and smoked an occasional cigar, 60 had regularly smoked cigarettes, and the other 2 a pipe or cigars. Apart from the one asbestos worker mentioned, none of the 63 men had worked in an occupation known to be associated with lung cancer.

After removal, the tracheobronchial tree was divided into 208 sections as described previously (see New Engl. J. Med., 1957, 256, 97; Abstr. Wld Med., 1957, 22, 5) and a sample of 55 sections from each patient was selected for study. The findings were recorded, using a punch-card technique for statistical analysis. The epithelium was examined, and if it was not normal in appearance it was described by recording the following characteristics: the presence or absence of cilia; the proportion of cells of each type present; the average thickness or number of cell rows; the length of the lesion; and the number of lesions of the same type in the section. The underlying tissue was also studied.

The 3 principal types of epithelial change recorded were an increase in the number of cell rows, a loss of cilia, and the presence of atypical cells. Each of these variables increased rapidly with the number of cigarettes smoked, with respect to both the number of sections showing the change and also the degree of change. In sections from non-smokers such lesions as were found generally showed only one of the 3 types of change. Amongst non-smokers there was no lesion composed entirely of atypical cells with cilia absent. In sections from men who had smoked 2 or more "packages" of cigarettes a day or who had died of lung cancer atypical cells were almost always present. [A package presumably contains 20 cigarettes.] The most striking lesions (apart from invasive carcinoma) were composed entirely of atypical cells with cilia absent, the great majority being 5 or more cell rows in average

depth. Such lesions were found in 4.3% of sections from men who smoked 1 to 2 packages a day, in 11.4% of sections from those who smoked 2 or more packages a day, and in 15% of sections from those who died of lung cancer. None was found among men who never smoked regularly, and very few among light smokers. [The paper contains a great number of figures and analyses concerning the 22,110 slides examined during the course of the investigation.]

The authors consider it justified to apply the term "carcinoma in situ" to the lesions composed entirely of atypical cells with cilia absent. They conclude that the histological evidence from this study greatly strengthens the body of epidemiological evidence that cigarette-smoking is a major factor in the causation of bronchogenic carcinoma.

G. Clayton

279. The Collagen and Elastin Content of the Lung in Emphysema

J. A. PIERCE, J. B. HOCOTT, and R. V. EBERT. Annals of Internal Medicine [Ann. intern. Med.] 55, 210-222, Aug., 1961. 9 figs., 20 refs.

The authors, at the University of Arkansas Medical Center, Little Rock, have compared the morphology and results of chemical analysis of emphysematous lungs with those of a control group of non-emphysematous lungs from patients of similar ages. Whole lungs taken at necropsy were extracted in 0.1 N NaOH for 7 to 14 days at room temperature. The lungs were then dried and sagittal cuts examined, the degree of emphysema being assessed from the size of air spaces and the extent of involvement. Each lung was then divided into 4 to 6 separaté blocks for analysis. Collagen and elastin were estimated from the results of autoclaving, whereby collagen becomes dissolved and elastin remains insoluble. Two-dimensional paper chromatograms were also made and hydroxyproline and valine contents estimated. The results showed that the collagen and elastin contents of the lungs were not markedly different whether emphysema was present or not; and, further, that there was no correlation between the collagen; elastin ratio and the severity of emphysema. It is therefore concluded that pulmonary emphysema does not result from loss of lung collagen or elastin. G. Loewi

280. Virus Pneumonia in Children during the 1958-9 Epidemic in Peking. (О вирусных пневмониях у детей в период эпидемии 1958/59 г. в Пекине) А. G. Вовкоу and Van Tin-De. Архив Патологии [Arh. Patol.] 23, 41-47, No. 9, 1961. 4 figs., 22 refs.

This communication from the Hospital of Sino-Soviet Friendship, Pekin, analyses the results of necropsy performed on 104 children aged from under 1 month to 7 years who died of pneumonia during the epidemic which occurred in 1958-9 in Pekin. In 51 cases viral pneumonia was diagnosed on the strength of the histological findings, namely, the characteristic hypertrophy and dystrophy of the alveolar epithelium, the presence of inclusion bodies, mostly those of adenovirus, and the necrotic character of the pneumonic foci. (Bacteriological and virological investigations could not be carried out.) The

remaining 53 cases were apparently of bacterial actiology and were mainly due to staphylococci, Gram-negative bacilli, and unidentified organisms. The predisposing conditions were measles in patients with rickets and "hypertrophy" (65 cases), and more rarely whooping-cough, dysentery, and other infectious diseases.

A. Swan

281. Elastic Tissue of Normal and Emphysematous Lungs: a Tridimensional Histologic Study R. R. WRIGHT. American Journal of Pathology [Amer. J. Path.] 39, 355-367, Sept., 1961. 16 figs., 18 refs.

In introducing this study of the morphology of the elastic tissue in the normal and emphysematous lung, carried out at the University of California Medical School, San Francisco, the author points out the importance of the elastic tissue components in pulmonary ventilation, both in the normally functioning lung and also, when adversely affected, in the production of pulmonary disease. From subjects aged from 8 to 93 years 24. normal-lungs and 11 lungs with definite emphysema, obtained at operation or necropsy, were distended with Zenker's solution, fixed, and examined by a tridimensional microscopical technique. By this method_the normal diffuse and even distribution of the elastic tissue throughout the whole lung was demonstrated. In the lungs of older patients there was occasional patchiness of this distribution in small areas of localized emphysema, while similar areas occurred near anthracotic deposits in younger subjects. In emphysematous lungs there was a diffuse disorganization and destruction of elastic tissue, together with degenerative changes in the remaining pulmonary structure. The damage to the elastic tissue was considered to be especially important.

J. B. Wilson .

282. Fixed and Reproducible Orthostatic Proteinuria.

I. Light Microscopic Studies of the Kidney

R. R. Robinson, S. N. Glover, P. J. Phillippi, F. R. Lecoco, and P. R. Langelier. *American Journal of Pathology [Amer. J. Path.*] 39, 291–306, Sept., 1961. 16 figs., 22 refs.

At the U.S. Air Force Hospital, Lackland, Texas, 56 young trainees (mean age 19 years) with fixed and reproducible orthostatic proteinuria were studied. In all cases specimens of renal tissue were obtained by percutaneous left renal biopsy and examined under the light microscope. One of the most consistent findings was an alteration in the filtration surfaces of the glomerular capillary loops, the main change being a thickening of the capillary wall (noted in 45% of cases), usually without involvement of the basement membrane. Also observed, however, were glomerular hypercellularity, slight capsular thickening, and the occurrence of small eosinophilic granules within the capsular space.

It is considered that this alteration in the epithelial component of the glomerulus was mainly responsible for permitting an increased transfer of protein, the haemodynamic factor playing only a "permissive" role. No definite tubular abnormalities were found and tubular changes were therefore not thought to play a part in the production of the syndrome.

J. B. Wilson

Microbiology and Parasitology

283. The Status of the Microscopic Diagnosis in the Epidemiology of Smallpox

N. S. DEODHAR. Indian Journal of Medical Sciences [Indian J. med. Sci.] 15, 517-528, July, 1961. 2 figs., 24 refs.

The author, writing from the B.J. Medical College, Poona, India, first reviews the incidence, virology, infectivity, and laboratory diagnosis of smallpox. He then describes his technicue for the investigation of cases of atypical smallpox and chickenpox by the smear test, that is, by the direct microscopical examination for smallpox virus of stained smears from skin lesions. He employs Paschen's method and gives details of the collection of specimens, preparation of smears, and laboratory procedures. A positive smear exhibits very large numbers of smallpox elementary bodies, which are typically globular, often paired, uniform in size, and readily detectable; although it does not distinguish between smallpox, vaccinia, and cowpox, it yields a strong presumptive diagnosis of smallpox. It differentiates between this disease and chickenpox, in which the virus is difficult to demonstrate and identify. The interpretation of positive, negative, and doubtful readings is discussed.

Clinical details are given of 31 cases of atypical smallpox or chickenpox investigated. The smear test was usually performed early in the illness. In 12 cases, all of which yielded a negative smear, the final clinical diagnosis was chickenpox. In the other 19 cases the smear test was positive and the final clinical diagnosis was smallpox. Positive results were obtained in 5 cases at the papular stage, in 10 at the vesicular stage, in 3 with sparse lesions, and in one, examined at the 10th day. with pustules. In 6 instances the diagnosis of smallpox would have been missed, at least in the early stages, but for the smear test. Two of these patients had only sparse lesions and 4 had been provisionally diagnosed as chickenpox; their early and rapid diagnosis as smallpox allowed control measures to be instituted without delay.

The author makes a plea for the more extensive use of the smear test in the diagnosis of smallpox. In the control of this disease prompt diagnosis is necessary, not only of typical cases, but also of atypical, mild, or modified cases which, if missed or misdiagnosed, may remain as infective sources in the community. The simplicity, rapidity, reliability, and economy of the smear test make it particularly suitable for use in countries such as India with a high incidence of smallpox, but with limited laboratory facilities and personnel.

Joyce Wright

284. Monitoring Sterilization of Dressings in High-vacuum Pressure-steam Sterilizers

R. J. FALLON. Journal of Clinical Pathology [J. clin. Path.] 14, 666-669, Nov., 1961. 3 figs., 5 refs.

285. The Nature of the Hemagglutinating Agent Noted in the Blood Serum of Patients with Viral Hepatitis R. E. HOYT, L. M. MORRISON, and M. G. LEVINE. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 104-106, July, 1961. 6 refs.

The authors have previously reported the agglutination of the erythrocytes of rhesus monkeys by the serum of patients with infective hepatitis (J. Lab. clin. Med., 1957, 49, 774; Abstr. Wld Med., 1957, 22, 424), and this was later confirmed by Rubin et al. (Science, 1957, 126, 1117).

In this paper from the College of Medical Evangelists, Los Angeles, they describe experiments undertaken to determine whether the phenomenon is due to a haemagglutinating virus in the patient's blood or to an antibody developing in the course of the illness. The procedure was as follows. Rabbits were immunized with the monkey erythrocytes which had been agglutinated by serum from cases of infective hepatitis and washed. The resulting antisera were tested for antiglobulin antibody with human Group-O Rh-positive erythrocytes sensitized with human anti-Rh blocking serum.

In 3 rabbit antisera, each deriving from the serum of one case of infective hepatitis, the titres with the human sensitized cell's were respectively 1:16, 1:8, and 1:32, whereas pre-immunization sera from the same rabbits gave no reaction. These results indicated that antiglobulin antibody had developed in the rabbits during immunization; from this it followed that antigen adsorbed upon the monkey erythrocytes from the infective sera must have been globulin in nature, and not virus. Similar results were obtained when rabbits were immunized with sheep erythrocytes agglutinated with sera from 3 cases of infectious mononucleosis and then washed. The titres in the 3 rabbit antisera, when tested for antiglobulin antibody with human sensitized cells were respectively 1:128, 1:32, and 1:64, the corresponding titres in these sera before immunization being 1:2, negative, and 1:4.

This similarity in immunological response in rabbits in relation to the two diseases indicates that the mechanism of agglutination of animal erythrocytes by sera from cases of both infective hepatitis and infectious mononucleosis is the same and involves a gamma-globulin fraction in the patient's serum. In the latter disease the agglutinating agent has the attributes of an antibody, and the present observations suggest that a similar antibody, and not a virus, is responsible for the agglutination of *Macacus rhesus* erythrocytes by infective hepatitis serum.

The rationale of the experimental work is clearly explained and particulars of the laboratory procedures are given.

Joyce Wright

Pharmacology and Therapeutics

286. A Measure of the Effectiveness of Propoxyphene Antitussives in Children

C. M. GRUBER JR. and C. H. CARTER. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 443-447, Oct., 1961. 2 figs., 3 refs.

The comparative antitussive effects of L-propoxyphene oxide hydrochloride and L-propoxyphene 2-naphthalene sulphonate were studied in 44 children with cough associated with acute respiratory tract disease, half of whom received the former drug and half received the latter. Both drugs were given by mouth in a dosage of 25 to 100 mg. 4 times daily. The efficacy of the drugs was assessed from the patients' answers to a questionary. The two drugs were equally potent as antitussives, but the oxide had a much smaller anti-expectorant effect than the sulphonate.

V. J. Woolley

287. The Effect of Prethcamid in Respiratory Failure. [In English]

P. LUND-JOHANSEN. Acta medica Scandinavica [Acta med. scand.] 170, 141-149, Aug., 1961. 7 figs., 21 refs.

The effect of "prethcamid" ("micoren") [equal parts of crotethamide and cropropamide] on ventilation and continuously recorded arterial oxygen saturation has been tested in patients with chronic respiratory failure. Single intravenous injections of 225 mg. micoren induced a distinct, but short-lasting increase in the tidal volume, minute volume and the arterial oxygen saturation. During intravenous infusions of 800 to-1,600 mg. per 30 to 120 minutes it was possible to induce and maintain a considerably increased oxygen saturation and clinical improvement in severely ill patients. In conscious patients disagreeable, but short-lasting side-effects were frequent. Trials with intramusculár and oral administration showed no distinct effect.

In 2 cases with acute respiratory failure (one after anaesthesia and one after morphine) injections of micoren seemed to be of life-saving effect.—[From the author's summary:]

288. A Comparison of the Properties of Chlorothiazide, Spironolactone and a Combination of Both as Diuretic Agents

D. A. OGDEN, L. SCHERR, N. SPRITZ, and A. L. RUBIN. New England Journal of Medicine [New Engl. J. Med.] 265, 358-362, Aug. 24, 1961. 4 figs., 39 refs.

A study to determine the relative effectiveness of chlorothiazide, spironolactone, and a combination of both drugs as diuretic agents is reported from Cornell University Medical College, New York. Of the 13 patients taking part, 10 had cirrhosis of the liver with ascites and 3 congestive heart failure; in all 13 cases moderate to severe retention of fluid was present. The patients received chlorothiazide, 0.5 g. twice daily, or spironolactone, 100 to 200 mg. 4 times daily, or a combination of the 2 drugs in this dosage. Chlorothiazide alone

caused a diuresis in 4 out of 12 cases, accompanied by loss of weight; the diuresis caused by spironolactone alone (5 out of 10 cases) was accompanied by a greater loss of weight, and that following the combined treatment (7 out of 9 cases) by a still greater loss of weight. There was a fall in plasma potassium level in all the cases treated with chlorothiazide, a rise in 7 out of 10 of the spironolactone-treated cases, and a rise in 4 and a fall in 2 of those receiving the combination.

It is emphasized that excessive loss of potassium is especially likely to occur when diuresis does not follow chlorothiazide treatment, and that frequent determinations of plasma potassium concentration are necessary to guard against cardiac arrhythmias and hepatic encephalopathy.

V. J. Woolley

289. The Treatment of Inflammatory Diseases of the Peripheral Nervous System and Muscles with Rozental's Iodine Paste. (Лечение воспалительных заболеваний периферической нервной системы и мышц йодпастой Розенталя)

N. I. Andrejaškin. *Клиническая Медицина [Klin. Med. (Mosk.)]* **42**, 79–82, Sept., 1961. 2 refs.

Rozental's iodine paste consists of 3 parts of iodine, 20 parts of rectified alcohol, 30 parts of paraffin, and 150 parts of chloroform. In a trial described by the author the paste was applied to the skin over the painful nodes and the relief was almost instantaneous. The best results were obtained in acute conditions, particularly when the paste was applied in the early stages of the disease. The treatment was less successful, although still giving some relief, in brachial neuritis and facial and occipital neuralgia.

A. Orley

290. An Experimental Study of the Behavioural Effects of isoThipendyl Hydrochloride (Theruhistin). [In English] L. Uhr and J. G. Miller. Acta allergologica [Acta allerg. (Kbh)] 16, 141-150, 1961. 8 refs.

The effect on behaviour of a new antihistamine, isothipendyl hydrochloride ("theruhistin"), was studied in a double blind trial on 26 volunteers. A dose of 8 mg. (double the normal dose of 4 mg.), was given and 40 objectively measured variables were scored from a number of behavioural tests of driving skill, simple psychomotor performance, vision, steadiness, attention, alertness, and tempo. No drug effects were observed on any of the 40 objective scores. A single subjective score "activity" was influenced at the 1% level of significance by the drug, which led to "feelings of greater activity".

A. W. Frankland

291. Pharmacological Study of Glycyrrhizin M. L. Gujral, K. Sareen, D. P. Phukan, and M. K. P. Amma. *Indian Journal of Medical Sciences [Indian J. med. Sci.*] 15, 669-775, Oct., 1961. 17 refs.

Chemotherapy:

292. Effect of a New Antiviral Drug (Xenalamine) in the Treatment and Prophylaxis of Various Diseases in Childhood. (Azione di un recente antivirale di sintesi (xenalamina) nella terapia e profilassi di alcune forme morbose in età pediatrica)

L. Magni. Minerva medica [Minerva med. (Torino)] 52, 2760-2770, Aug. 18, 1961. 12 figs.

The author reports from the Ospedale al Mare, Venice, a trial of a recently introduced synthetic antiviral drug ("xenalamine"). In 48 out of 58 young children with influenza the drug proved to be very effective, the temperature falling rapidly and the pulmonary signs quickly subsiding. In the remaining 10 patients who had septic and toxic complications, however, the drug was of no avail. No untoward side-effects were observed in spite of prolonged treatment, and all the patients tolerated the drug well.

The drug was then tested for its therapeutic and prophylactic value in measles and chickenpox, being given therapeutically in a dosage of 50 mg. per kg. body weight for 10 days and prophylactically in a dosage of 80 mg. per kg. for 25 to 30 days. Clinically, the course of both diseases in most cases was mild and of short duration. While good results were obtained in the prophylactic treatment of measles, the results in chickenpox were doubtful and uncertain. The chemotherapeutic action of this drug seems to be based on the changes it produces in the cellular structure which influence the reproduction of the virus and attenuate its virulence.

293. Studies with Monopropionyl Erythromycin J. Syme, J. Downie, and J. McC. Murdoch. Scottish Medical Journal [Scot: med. J.] 6, 376-380, Aug., 1961. 2 figs., 20 refs.

Monoesters of erythromycin have been synthesized in an attempt to obtain an antibiotic the administration of which is followed by fewer toxic effects and higher and more predictable blood levels than with erythromycin. At the City Hospital, Edinburgh, erythromycin propionate was given by mouth to 50 patients suffering from predominantly coccal infections in a dose of 250 mg. every 6 hours (a smaller dose in children). Of 37 patients with bronchopneumonia who received the antibiotic for 7 to 10 days, the result was "good" in 31—that is, temperature, pulse rate, and leucocyte count became normal within 72 hours; in 5 the result was "moderately good". and in one patient, a child with bronchopneumonia complicating measles, it was poor. Of a group of 6 patients with acute otitis media, also treated for 7 to 10 days, the results were good in 5 and moderate in one. Of 7 patients with staphylococcal infections such as septicaemia (1), cellulitis (1), and osteomyelitis (5), who received the antibiotic for periods up to one month, the results were good in 5. The only toxic effect was diarrhoea, which occurred in 2 children only, the incidence of toxic effects comparing favourably with that of erythromycin base.

A comparison in 10 patients of the serum concentrations of erythromycin after administration of the stearate and the monopropionyl ester showed that the serum levels were much higher 2 and 6 hours after the fourth dose of the monopropionyl ester than after the same dose of erythromycin stearate. The serum levels of both preparations were above that $(0.25 \, \mu \text{g}. \text{per ml.})$ required for bacteriostasis and the level of the monopropionyl ester almost reached the bactericidal level of 5 $\mu \text{g}.$ per ml.

On the basis of these findings monopropionyl erythromycin is recommended in the treatment of Gram-positive coccal infections.

T. B. Begg

294. The Treatment of Severe Staphylococcal Infections with Vancomycin

D. W. Woodley and W. H. Hall. Annals of Internal Medicine [Ann. intern. Med.] 55, 235-249, Aug., 1961. 6 figs., 22 refs.

A trial of vancomycin in the treatment of 25 cases of severe staphylococcal infection is described in this paper from the Veterans Administration Hospital and the University of Minnesota Medical School, Minneapolis. Vancomycin is an antimicrobial agent produced from strains of Streptomyces orientalis and is active primarily against Gram-positive organisms, including penicillinresistant staphylococci. It has been shown to be effective in staphylococcal septicaemia when all other antibiotics have failed. Further, there is no report in the literature of the emergence of staphylococci showing resistance to vancomycin.

Usually a saline infusion of the drug was given intravenously, the dosage being 1 g. in 30 minutes every 12 hours. In intestinal infections 500 mg. was given by mouth every 6 hours. Toxic effects, which have also been observed by other workers, included thrombophlebitis, drug fever, skin rashes, perceptive nerve deafness, and anaphylactic shock, but the incidence of the last two was low. It is emphasized that before administration of the drug it must be established that renal function is satisfactory.

The conditions treated in the present series included staphylococcal septicaemia, pneumonia, endocarditis, and enterocolitis. The authors state that the most dramatically successful results were obtained in enterocolitis, although there was no doubt that the drug could be considered life-saving in some of the other cases. In their view vancomycin is the drug of choice in severe penicillin-resistant staphylococcal infections. [This may not now be correct since the advent of the new penicillins which are far less toxic than vancomycin.]

J. S. Malpas

Infectious Diseases

295. A New Single-dose Piperazine Preparation for the Treatment of Enteroblasis

R. A. EIDAL, G. D. WILDE, G. G. THOMAS, F. L. HAEN, and R. I. SHAPARD. *Journal of New Drugs* [J. New Drugs] 1, 122-125, May-June [received Sept.], 1961. 14 refs:

The authors of this paper from the Doctor's Clinic, Auburn, Washington, report a trial of "pripsen", a combination of piperazine and extract of senna pod, in the treatment of enterobiasis. A single dose of the drug (ranging from 1 g. in children under 4 years of age to 4 g. in adults) was given to 30 patients, including both parents in each of 8 families and 14 children in these families. Starting one week after treatment perineal swabs were taken daily for 7 days and examined for evidence of pinworm infection. The criterion of cure was a negative swab on all 7 days; if only one swab was positive treatment was considered to be a failure. Of the 30 patients, 28 were cured by the single dose; the remaining 2 required a further single dose.

About two-thirds of the patients complained of fleeting abdominal discomfort, but there were no other side-effects. It is pointed out that in this method of treatment a considerably smaller total dose of piperazine is necessary than when piperazine is given alone in divided doses—namely, 4 g. as a single dose in an adult compared with 19 g. of piperazine over a period of 7 days.

E. H. Johnson

VIRAL DISEASES

296. Varicella Pneumonia

R. H. Mermel Stein and A. W. Freireich. Annals of Internal Medicine [Ann. intern. Med.] 55, 456-463, Sept., 1961. 4 figs., 28 refs.

Between January, 1953, and July, 1960, a total of 38 patients with varicella were admitted to Meadowbrook Hospital, Hempstead, New York. In 13 of these (9 males and 4 females, aged 20 to 47 years) the condition was associated with pneumonia. Although few physical signs of pneumonia were detected, respirations were often rapid and shallow. In 4' cases pneumonia was diagnosed only after radiological examination of the chest. The authors suggest that the incidence of pneumonia complicating varicella may be higher than was previously thought to be the case, and that this complication would be diagnosed in many more cases were radiological examination carried out as a routine. Most of the patients in this series received penicillin combined with another antibiotic; corticosteroids were not given: There were no deaths.

In a discussion the authors state that the pneumonia usually occurs between the second and sixth days of the illness and that adults are predominantly affected. The manifestations range from cough, chest pain, and slight

dyspnoea to haemoptysis, shock, and cyanosis. The chest radiograph shows diffuse punctate and small nodular opacities throughout the lungs, with relative sparing of the apices. In the perihilar regions strand-like densities blend with the shadows of the hilar lymph nodes. Treatment, which is supportive, includes administration of antibiotics and oxygen. Steroid therapy is "probably indicated where there is evidence of adrenal collapse or when the outcome is in doubt". Regression of the process begins within one week and is usually complete within 2 weeks. Pericarditis, encephalitis, and nephritis may develop in fulminating cases. The prognosis is poorest in cases of varicella pneumonia complicating pregnancy. Necropsy may reveal bronchopneumonia with suppuration, and Type-A inclusion bodies may be found in the mononuclear cells of the pulmonary exudate. A. Garland

297. An Outbreak of Asian Influenza amongst Men and Horses. (Вспышка гриппа A₂ среди людей и лошадей (Предварительное сообщение))

Z. V. DOMRAČEVA. Журнал Микробиологии Эпидемиологии и Иммунобиологии [Ž. Mikrobiol. (Mosk.)] 32, 31–36, July, 1961. 4 refs.

The author has investigated an outbreak of influenza among the men and horses at the Central Hippodrome, Moscow, which began early in January, 1959, at the same time as there was an outbreak among the population of the city. During the period of the investigation about 50% of the staff and 22.4% of the horses fell ill with influenza-like symptoms. Specimens of nasopharyngeal washings or swabs and samples of serum, the latter paired whenever possible, were collected, the washings being inoculated into chick embryos by the amniotic route and the sera tested for neutralization and haemagglutination inhibition (Hirst).

From 35 washings obtained from the staff and 88 swabs from horses 13 strains with hacmagelutinating properties were isolated, of which 5 were derived from human and 8 from equine infections. Examination of 3 of these strains in greater detail showed that Strain 92 (human) and Strain 41 (equine) corresponded closely to several influenza strains of the Asian type (A2 in the Russian terminology), while Strain 27 was more nearly related to the influenza virus Strain A56 (Prague). Further, paired sera from 18 cases of human influenza and 22 cases in horses were examined by the same techniques. When tested against laboratory strains of the Asian type of influenza virus-positive results were obtained with 50% of both the human and equine paired sera, and the antibodies against Asian influenza virus thus demonstrated in the sera showed a rising titre in the second of the paired sera. When the newly isolated human Strain 92 and the equine Strain 41 were used as antigens, antibodies against these strains, again with rising titres, could be demonstrated in 88% of both

human and equine paired sera. These results are considered to establish the fact that influenza-like illness in horses may be caused by human strains of Asian influenza virus.

K. Zinnemann

298. Mortality from Varicella in Children Receiving Adrenocorticosteroids and Adrenocorticotropin K. C. Finkel. *Pediatrics* [*Pediatrics*] 28, 436-441, Sept., 1961. 17 refs.

The author reports an inquiry into the mortality among children who developed chickenpox while receiving steroid therapy for a variety of other medical conditions. He has collected 44 such cases, of which 7 were seen by him at the Children's Hospital, Winnipeg, while details of the remaining 37 were obtained from various other centres in Canada and the U.S.A. in response to postal inquiry. The patients' ages ranged from 1 to 15 years. There were 6 deaths in the series, 5 among 12 children suffering from leukaemia (in 11 cases acute and in one chronic), while another death occurred in a patient with Letterer-Siwe disease. In addition to steroids all these patients had also been treated with gamma globulin, the folic acid antagonist "methotrexate", or cytotoxin (2 cases each). The steroids used were prednisone in 23 cases, ACTH (corticotrophin) in 8, cortisone in 6, dexamethasone in 3, hydrocortisone and triamcinolone in one case each, and both ACTH and cortisone in one; the steroid given in the case of chronic leukaemia is not mentioned. The dosage of steroid, expressed in mg. of cortisone per unit body weight per 24 hours, ranged from 1 to 7 mg. per lb. (2.2 to 15.4 mg. per kg.). In the fatal cases the range was 4.4 to 13.2 mg. per kg. body weight during the preceding 14-day incubation period and also during the first 4 days of the exanthem. In 21 cases steroids were stopped at the onset of the eruption. The duration of the varicella ranged from 4 to 14 days in most cases.

The author considers that many of the deaths that occur in patients receiving steroids are more likely to be due to the effects of the underlying disease on immune mechanism rather than to the steroids themselves, especially in leukaemia when the natural resistance to infection is impaired, particularly during a relapse of the disease. Most of the other physicians replying to the inquiry held the view that steroids should be stopped only in patients with diseases involving the reticulo-endothelial system and that in other conditions in which there is less risk of harm the dosage need only be reduced to a maintenance level equivalent to 25 to 50 mg. of cortisone daily.

[The points raised in this review are important and the paper should be read in full.]

I. M. Librach

299. Prospects for Measles Immunization with Reference to the Relationship between Distemper and Measles Viruses

V. J. CABASSO, S. LEVINE, F. S. MARKHAM, and H. R. Cox. *Journal of Pediatrics* [J. Pediat.] 59, 324-338, Sept., 1961. 35 refs.

At the Lederle Viral and Rickettsial Research Laboratories, Pearl River, New York, the authors have investigated the relationship between the canine distemper and measles viruses by cross-immunological experiments in various animals and tissue culture, some investigators having suggested the use of a modified distemper virus for the protection of children against measles. The investigations failed, however, to confirm such a relationship. While effective protection against measles by the administration of distemper virus is thus questionable, the vaccination of children with attenuated measles virus has been shown to produce measles antibodies, even when the concentration of virus administered is only 6 TCD₅₀. A group of 22 children whose ages varied from 1 to 8 years, selected as being susceptible to measles, received a single subcutaneous injection of 1 ml. of a vaccine containing 100 TCD₅₀ of virus per ml. The children's serum was tested before and after the vaccination. Two children showed significant levels of neutralizing antibodies before the injection, and all the others developed neutralizing antibody after the vaccination. Among the clinical reactions, which were similar to those in measles modified with γ globulin, fever occurred in 17 of the 20 patients, while rash, Koplik spots, and catarrhal signs were recorded in many fewer cases. The affected children were neither in a toxic state nor acutely ill. No virus was recovered either from the nasopharynx or the blood and no case of secondary measles occurred. Questions such as the duration of immunity, the ability of vaccinated children to transmit the infection, and possible complications such as postvaccination encephalitis need further examination. Franz Heimann

300. Giant Cell Pneumonia and Measles: an Analytical Review

D. T. Janigan. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 741-749, Sept. 23, 1961. 11 figs., bibliography.

BACTERIAL DISEASES

301. Treatment of Tetanus: with Special Reference to Tracheotomy

P. M. SMYTHE and A. B. BULL. British Medical Journal [Brit. med. J.] 2, 732-736, Sept. 16, 1961. 15 refs.

A series of 55 children, excluding cases of tetanus neonatorum, were admitted to Groote Schuur and the Red Cross War Memorial Children's Hospitals, Capetown, with tetanus between 1951 and 1957. The invasion period could not be accurately determined in many cases, but in 26 of them it was less than 48 hours. Treatment consisted in the intravenous and intramuscular injection of tetanus antitoxin and the administration of penicillin, barbiturates, paraldehyde, and, in a few cases, chlorpromazine. Of these 55 patients, 27 (49%) died. A further series of 27 children with tetanus have been admitted to the same hospitals since 1958, the invasion period being 48 hours or less in 14 cases. In this series tracheotomy was performed in 14 cases and intermittent positive-pressure respiration (I.P.P.R.) was used in 4 cases. Of these 27 children, 3 (11%) died. With the exception of tracheotomy and I.P.P.R. treatment was essentially the same in both groups apart from the use of mephenesin in some of the more recent cases; mephenesin

was administered together with phenobarbitone by stomach tube, and this appeared to be more effective than other combinations of drugs.

. In the more recent series tracheotomy was performed on all patients with frequent or prolonged spasms, laryngospasm, pharyngospasm or any difficulty in swallowing, or with signs of cardio-respiratory distress with a rising pulse rate, cyanosis, and sweating. It was invariably performed under general anaesthesia with the use of an endotracheal tube. A very "low" tracheotomy was found not to be entirely satisfactory and the authors consider that such tracheotomies are associated with a higher incidence of mediastinal emphysema and pneumothorax and with the making of false passages due to greater difficulty when the tracheotomy tube has to be changed. A Radcliffe tracheotomy tube was inserted initially when size permitted, as I.P.P.R. might be needed in cases which at first appeared to be only moderately severe. The necessity for adequate humidification is strongly emphasized. The tracheotomy tube was not removed until after the patient became able to swallow all feeds without difficulty and spasms had ceased to affect respiration. Aspiration of secretions from the trachea through the use of tracheotomy resulted in pulmonary infection becoming most uncommon; routine antibiotic therapy was discontinued after 10 days and subsequently given only if there was overt evidence of infection. Of the 3 fatal cases in the later series, in one the tracheotomy tube was apparently lying badly in the trachea from the outset, in the second death resulted from an occlusive tracheobronchitis, and the third death occurred because a connexion worked loose on the 14th day.

The authors conclude from the results of this study that even if I.P.P.R. is available tracheotomy and sedation should be tried first. They consider that I.P.P.R. should be begun only if tracheotomy and sedation fail, as indicated by the occurrence of: (1) severe spasms interfering with respiration and uncontrollable by sedation or requiring such heavy sedation as to depress respiration; (2) respiratory failure; or (3) hyperpyrexia of over 104° F. (40° C.) or increasing cardio-respiratory distress which, if it were allowed to continue, would result in collapse.

R. G. Meyer

302. Intermittent Positive-pressure Respiration in Tetanus

R. WRIGHT, M. K. SYKES, B. G. JACKSON, N. M. MANN, and E. B. ADAMS. *Lancet* [Lancet] 2, 678-680, Sept. 23, 1961. 16 refs.

In 1953 Bjørnboe and colleagues (Ugeskr. Læg., 115, 1535) introduced a technique of treating tetanus by means of total curarization and intermittent positive pressure respiration (I.P.P.R.). This technique has been used in the treatment of 25 cases of severe tetanus neonatorum at the King Edward VIII Hospital, Durban, and the results obtained compared with those in a group of 25 similar patients who were treated more conservatively and whose spasms were controlled by acetylpromazine or chlorpromazine, with the addition of soluble phenobarbitone when necessary, the patients being allocated to one or

other treatment group at random. In the patients treated with I.P.P.R. paralysis was produced by suxamethonium and then maintained by intramuscular injections of 3 mg. of p-tubocurarine (maximum daily dose to 48 mg.). Tracheal intubation was followed by tracheotomy and I.P.P.R., tracheal aspiration being performed bourly, or more often if secretions were profuse.

In this group 11 of the 25 patients died, a mortality of 44%, compared with 84% in the controls (21 deaths). Some of the deaths in the I.P.P.R. group were due to faulty technique in the early cases, 6 of them occurring among the first 8 patients; in the controls the main cause of death was bronchopneumonia and respiratory failure. The duration of curarization ranged from 12 to 16 days. The tracheotomy tube was usually removed shortly afterwards, often preceded by a period of "assisted respiration". The method of treatment with I.P.P.R. and curarization is recommended only for severe cases of tetanus and in units which deal with large numbers of such cases and where sufficient technical experience is available. (An addendum reports that in a further 18 cases there were only 2 deaths, a mortality of 11%.) John-Lorber :

303. Neonatal Tetanus in New Guinea: Effect of Active Immunization in Pregnancy

F. D. Schoffeld, V. M. Tucker, and G. R. Westbrook. British Medical Journal [Brit. med. J.] 2, 785-789, Sept. 23, 1961. 12 refs.

The authors report that the incidence of neonatal tetanus among the Abelam people of the Sepik District in New Guinea was found to be not less than 80 per 1.000 live births. Because of the strict taboos associated with childbirth among these people it was not possible to alter the circumstances of labour and delivery, and an attempt was therefore made to transfer passive immunity to the infant by active immunization of the mother during pregnancy. The plan was to give three injections of fluid formalinized tetanus toxoid, the third in the last trimester of pregnancy; however, for various reasons, including far advanced pregnancy, it was possible to give only one or two injections in many cases. In one group of 160 mothers who received one or no injection 16 (10%) of their babies developed neonatal tetanus, while of the babies of 234 women who received 2 injections, 8 (3.42%) did so. In contrast, in the final group of 175 women who received 3 injections only one baby (0.57%) developed neonatal tetanus.

The authors propose to give a booster injection of fluid toxoid to immunized women in future pregnancies. There were no adverse reactions and the cost was not high. It is recommended that active immunization against tetanus be given to all pregnant women in areas where neonatal tetanus is prevalent.

Winston Turner

304. Chlorpromazine in Tetanus

K. S. Kochhar. British Medical Journal [Brit. med. J.] 2, 789-790, Sept. 23, 1961. 6 refs.

Chlorpromazine has been used extensively in the treatment of tetanus. This paper from the Medical College, Amritsar, India, reports a clinical trial undertaken to

assess the comparative value of paraldehyde and chlorpromazine in the control of the tetanic spasms. Of the 170 patients in the trial, 89 were treated with paraldehyde and 81 with chlorpromazine in addition to a standard regimen of treatment. The spasms were more rapidly controlled by chlorpromazine than by paraldehyde, but the mortality was the same with both drugs.

Winston Turner

305. Control of a Staphylococcal Epidemic under Adverse Conditions

V. H. Bowers and J. R. Rose. British Medical Journal [Brit. med. J.] 2, 1044-1046, Oct. 21, 1961. 1 fig.

The authors of this paper from the South-East Kent Hospital Group describe the measures which rapidly brought under control without any form of segregation, isolation, or barrier-nursing technique a severe epidemic of cutaneous infections due to Staphylococcus pyogenes (Phage Types 80 and 3B/3C+) in a unit of 30 mentally subnormal but mostly active male children aged 6 to 15 years. It is hoped that since there were inadequacies of staff, equipment, and premises (the unit was part of an upgraded Poor Law Institution) the success achieved will be an encouragement to others.

The measures taken included: (1) weekly swabbing of the noses of patients and staff; (2) autoclaving weekly for 30 minutes at 5 lb. per sq. inch (350 g. per sq. cm.) all blankets (wool), mattresses, and pillows, the patients' clothing being similarly autoclaved initially; (3) laundering all curtains and cleaning of all rooms, an antiseptic being used for the walls and floors; (4) replacing enamelled chamber-pots by others of plastic material; (5) wiping all baths, basins, lavatory pans and seats, and chamber-pots after use with "savlon" 1 in 200; (6) sponging each patient all over after a bath using a flannel -different for each patient-soaked in 1 in 5,000 "hibitane" (chlorhexidine); (7) using hexachlorophene ("cidal") soap for washing and bathing; and (8) applying antiseptic ointment twice daily into both nostrils of all staff and patients, "neobacrin" being used for 2 weeks after which "naseptin" cream was substituted.

The number of lesions fell in a month from 41 to 8. After 3 months some of the measures were relaxed except in patients with lesions; there was an immediate increase in the number of new lesions, but resumption of the use of "naseptin" cream and of sponging with hibitane again brought about a decline in the number of new lesions.

A. Ackroyd

306. Controlled Studies of Streptococcal Pharyngitis in a Pediatric Population. 1. Factors Related to the Attack Rate of Rheumatic Fever

A. C. Siegel, E. E. Johnson, and G. H. Stollerman. New England Journal of Medicine [New Engl. J. Med.] 265, 1 559-566, Sept. 21, 1961. 27 refs.

Of 2,545 children coming to the out-patient clinic of the Children's Memorial Hospital, Chicago, because of nasopharyngitis, 1,213 (47.7%) were found to be harbouring β -haemolytic streptococci in the throat. Of these strains, 86% were Group-A streptococci, but only 52% could be typed serologically. Approximately half the patients

from whom throat cultures positive for β -haemolytic streptococci were obtained were treated with a single intramuscular injection of 600,000 units of benzathine penicillin, while the other half were treated symptomatically. Of 608 patients in the control group, rheumatic fever developed in 2 (0.33%) and acute glomerulo-nephritis in one (0.17%). No similar complications occurred in the 605 children in the penicillin-treated group.

The streptococcal disease was generally mild, which would account for the low attack rate of rheumatic fever and nephritis. All the 3 cases with these complications occurred among the 85 control patients who had a more virulent infection as judged by clinical, bacteriological, and immunological criteria. Nevertheless, it was impossible to recognize these more severe cases in the acute phase on the basis of clinical criteria alone. It is concluded that the risk of rheumatic fever occurring after sporadic nasopharyngitis is conditioned by the epidemiology of the streptococcal disease encountered.

[This is an excellent study.] John Lorber

307. Controlled Studies of Streptococcal Pharyngitis in a Pediatric Population. 2. Behavior of the Type-specific Immune Response

A. C. SIEGEL, E. E. JOHNSON, and G. H. STOLLERMAN. New England Journal of Medicine [New Engl. J. Med.] 265, 566-571, Sept. 21, 1961. 21 refs.

The authors describe a study of the effect of penicillin therapy on the development of type-specific immunity in 166 of the children previously investigated [see Abstract 306] who were suffering from streptococcal pharyngitis due to infection with either Type 12 or Type 3, the two most common serotypes encountered. Infection with typable strains of Group-A streptococci was followed by the formation of type-specific antibody in 57 (70%) of the 82 patients not given penicillin, despite the relative mildness, epidemiologically, of the streptococcal infection. In contrast, penicillin therapy that terminated the carrier state suppressed the type-specific immune response strikingly; thus of the 84 patients given a single injection of 600,000 units of benzathine penicillin, antibody appeared in only 19 (23%). Duration of the convalescent carrier state was the most important factor correlating with the development of type-specific immunity. With the exception of the finding of pharyngeal exudate, the severity of other clinical symptoms or signs did not correlate well with formation of antibody.

Type-specific antibodies disappeared from the serum within 2 or 3 years in more than half the patients studied, and in two-thirds of them during the 4 years of the study. In view of this finding it is pointed out that in clinical practice the advantages of intensive penicillin therapy (namely, prevention of rheumatic fever, prevention of epidemic spread, and hence decrease of virulence of the strains of streptococci) must be weighed against its disadvantages (that is, suppression of type-specific immunity, the possibility of penicillin allergy, expense, and inconvenience), particularly as under epidemiological conditions the attack rate of rheumatic fever is extremely low.

John Lorber

Tuberculosis

308. Further Experience with D-Cycloserine in the Sanatorium Treatment of Pulmonary and Urogenital Tuberculosis. (Weitere Erfahrungen mit D-Cycloserin in der Heilstättenbehandlung bei Lungen- und Urogenitaltuberkulose)

K. H. STEINITZ. Schweizerische Zeitschrift für Tuberkulose und Pneumonologie [Schweiz. Z. Tuberk.] 18, 65-75, 1961. 6 refs.

From the Berne Sanatorium at Heiligenschwendi, Switzerland, the author reports his results with D-cycloserine in the treatment of 153 cases of pulmonary and 21 of urogenital tuberculosis. Almost all (96.5%) of the patients had previously been treated with other tuberculostatic drugs, two-thirds of them on more than one occasion. Some 70% of the patients were over 40 years of age, many being in their fifties and sixties, while 38% of them had one or more complications such as tuberculous bronchitis (30 cases), bronchial granulomata following resection (10 cases), and empyema (9 cases). Three patients had both urogenital and pulmonary tuberculosis. Non-specific complications were also common, and included myocardial insufficiency, cor pulmonale, hypertension, asthma, emphysema, and chronic bronchitis.

The indications for giving cycloserine were deterioration or insufficient or no progress in the patient's condition, the presence of strains resistant to other tuberculostatic drugs, or intolerance to these drugs. In 83.3% of the cases other antituberculous drugs were given in combination with cycloserine, usually isoniazid. The usual dose was 0.25 g. of cycloserine three times daily, phenobarbitone 0.1 g. daily, with latterly vitamin B_6 (pyridoxine) in addition.

Treatment was continued for an average of 113 days, and during this period 45% of cases became permanently bacteriologically negative. Definite radiological improvement was noted in 32.2% and slight improvement in a further 43%. Over half (52.3%) of the patients complained of some form of side-effect, vertigo being the most common, and in 32 cases the drug had to be withdrawn for this reason. In view of the advanced nature of the disease in these cases the results are considered encouraging, and the author has been led gradually to widen the indications for the use of cycloserine.

H. F. Reichenfeld

309. Corticotropin in the Treatment of Tuberculosis: a Controlled Study

J. H. Angel, L. S. Chu, and H. A. Lyons. Archives of Internal Medicine [Arch. intern. Med.] 108, 353-369, Sept., 1961. 2 figs., 42 refs.

The authors state that there have previously been only three strictly controlled studies of the value of the corticosteroids in the treatment of active pulmonary

tuberculosis. The results of these studies, which are briefly reviewed, have favoured this form of treatment. provided, of course, that the tubercle bacilli have not become drug-resistant. In the present study, reported from the State University of New York, Brooklyn, corticotrophin (ACTH) was used instead of the adrenal cortical steroids, since the latter are liable to cause postoperative collapse on withdrawal. Patients were accepted for the trial only if they had active, bacteriologically proved, pulmonary tuberculosis of recent origin, had not received previous antituberculous treatment for more than 3 weeks, and were free from vascular, cardiac, gastric, renal, adrenal, and mental disease. They were divided at random into (1) a control group of 50 patients who received streptomycin, PAS, and isoniazid in the usual dosages, and (2) 54 patients who were given the same drugs plus ACTH gel, the latter in an initial dosage of 60 units daily for 4 days, gradually reduced to 30. units daily, this drug being given for 13 weeks altogether: these patients were kept on a low-salt diet and given 2 g. of potassium chloride daily. The groups were comparable in regard to age and sex. The medical panel assessing the results were unaware to which group the patient belonged.

In nearly all the patients treated with ACTH there was a striking initial improvement in the clinical picture and 90% were afebrile within 48 hours. There was a more rapid gain of weight which was not lost on withdrawal of ACTH, suggesting that the increase was not due to fluid retention. There was some evidence that alcoholic patients did particularly well with ACTH. However, sputum conversion was more rapid in controls up to 6 months; on the other hand, radiological improvement was far more pronounced in the ACTH-treated group.

The authors stress again, however, the importance of the causative organism being still sensitive to drugs when ACTH is to be used.

Paul B. Woolley

310. Difficulties in the Diagnosis and Management of Unsuspected Tuberculous Enteritis and Colitis E. J. M. CAMPBELL. Gut [Gut] 2, 202-209, Sept., 1961. 1 fig., 9 refs.

The author, from the Middlesex Hospital, London, describes 6 cases in detail to draw attention to the difficulties in diagnosis of tuberculous enteritis and colitis. The chief method of diagnosis, by radiology, is shown to have underestimated or misinterpreted the true condition in 4 of the 6 cases. In 3 cases there were normal chest radiographs. Tubercle bacilli were found in the faeces in one case only. All the patients required both surgical and medical treatment. The clinical picture was variable, patients presenting the symptoms of pain, vomiting, diarrhoea, loss of weight, malabsorption, and anaemia.

Thomas Hunt

Venereal Diseases

311. Evaluation of the Fluorescent Treponemal Antibody (FTA) Test for Syphilis. Comparison with *Tre*ponema pallidum Immobilization (TPI) Test

E. H. FIFE JR., B. M. BRYAN, R. W. SANDERS, and L. H. MUSCHEL. American Journal of Clinical Pathology [Amer. J. clin. Path.] 36, 105-113, Aug., 1961. 18 refs.

The fluorescent treponemal antibody (F.T.A.) test was performed on sera sent to the Walter Reed Army Medical Center, Washington, D.C., for examination by the treponemal immobilization (T.P.I.) test: the first technique described by Deacon et al. (Proc. Soc. exp. Biol. (N.Y.), 1957, 96, 477; Abstr. Wld Med., 1958, 24, 26) was used, but the sera were incubated at room temperature instead of at 37° C. However, when the recommended serum dilution of 1 in 5 was used it was found difficult to differentiate moderately reactive from non-reactive sera owing to non-specific fluorescence. The authors therefore modified the procedure, first by rinsing the slides free from excess serum and antihuman globulin conjugate on a mechanical rotator, and later by testing sera at a dilution of 1 in 100. In 745 sera tested by the original method modified as described 90% agreement was obtained between the results of the F.T.A. and T.P.I. tests, 6% of the sera being reactive only with the F.T.A. test and 4% only with the T.P.I. test. Repeated tests on sera which gave discrepant results by the two procedures suggested that reproducibility was better with the F.T.A. than with the T.P.I. test.

It is possible that the result of the F.T.A. test may be affected by sensitization of the treponemes in vivo by antibody produced in the source animal (the rabbit) and therefore one of the essentials of the test is that the organisms should be harvested from the testes not more than 24 hours after the appearance of definite orchitis. To confirm this, F.T.A. tests were performed using as antigen a treponeme suspension obtained 7 days after the development of orchitis in the rabbit; this showed marked "sensitization" of the organisms and greatly reduced their activity with human syphilitis antibody, the reduction in titre being 8-fold compared with the titre obtained with an unsensitized suspension. This suggested that the sensitization of the treponemes by the rabbit antibody had exercised a blocking effect and prevented union with the antibody.

The authors consider that their results indicate that the F.T.A. test is more sensitive than, and at least as specific as, the T.P.I. test and relatively simple to perform. They find it a valuable adjunct to the latter, particularly when examining sera with threshold amounts of antibody or those showing non-specific immobilization which prevents a valid T.P.I. result being obtained.

A. E. Wilkinson

312. Treatment Problems of Gonorrhoea

R. R. Willox. Bulletin of the World Health Organization [Bull. Wld Hlth Org.] 24, 307-319, 1961.

313. Demethylchlortetracycline Hydrochloride in the Treatment of 267 Patients with Acute Gonorrhea: Results and Evaluation

J. R. Allison Jr. Antibiotics and Chemotherapy [Anti-biot. and Chemother.] 11, 454–460, July [received Sept.], 1961. 1 fig., 16 refs.

From the public health point of view it is considered that before a drug can be considered suitable for the primary treatment of acute gonorrhoea in patients seen at venereal disease (V.D.) treatment centres the following criteria must be satisfied: (1) the drug must be effective in a single dose; (2) potent antibacterial levels in the serum must be rapidly achieved; and (3) allergic reactions or serious side-effects must be minimal or absent.

At the V.D. Centre of the Richland County Health Department, South Carolina, demethylchlortetracycline hydrochloride was given in the primary treatment of 267 patients with acute gonorrhoea. Alternate patients were allotted to one of two treatment regimens and received either 4 or 6 capsules of the drug, each containing 150 mg., as a single oral dose, the capsules being swallowed under observation; no other treatment was given. Bloodlevels of demethylchlortetracycline were determined in 8 patients in each treatment group at 48, 72, and 120 hours and all patients were asked to return for examination after one week. Treatment was considered a failure when smears were positive on re-examination except in those cases in which there had been further contact with the original source of infection.

Of 110 patients given 600 mg. and re-examined, 92 (84%) responded well and of 128 given 900 mg., 119 (93%) were considered to be cured. Toxic side-effects, which were encountered in about 20% of patients receiving the lower dose and in 40% of those receiving 900 mg, were mainly gastro-intestinal disturbances which were usually mild and of short duration. No instance of anaphylaxis or skin reaction was observed.

In view of the apparent increase in anaphylactoid reactions after penicillin and the emergence of strains of Neisseria gonorrhoea which are resistant to that antibiotic the author considers that "it might seem advantageous to avoid penicillin therapy whenever possible". In his view demethylchlortetracycline is effective in the treatment of gonorrhoea and particularly valuable for use in V.D. treatment centres.

A. J. Gill

314. Gonococcal Resistance to Penicillin in the Light of Recent Literature

C. M. CARPENTER. Bulletin of the World Health Organization [Bull. Wld Hlth Org.] 24, 321-326, 1961. Bibliography.

315. Fluorescent Antibody Methods for Neisseria gonor-rhoeae Identification

W. E. DEACON. Bulletin of the World Health Organization [Bull. Wld Hlth Org.] 24, 349-355, 1961. 18 refs.

Tropical Medicine

316. O'Nyong-nyong Fever: an Epidemic Virus Disease in East Africa. IV. Vector Studies at Epidemic Sites P. S. Corbet, M. C. Williams, and J. D. Gillett. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med. Hyg.] 55, 463-480, Sept., 1961. Bibliography.

This is the fourth paper from the East African Virus Research Institute, Entebbe, Uganda, on this denguelike fever, differing from Chikungunya fever by the presence of lymphadenitis (see Trans. roy. Soc. trop. Med. Hyg., 1961, 55, 361; Abstr. Wld Med., 1961, 30, 445). The epidemic occurred in northern Uganda in 1959 and the examination of no less than 64 local arthropods in an attempt to discover the vector is described. Virus isolations had previously been made from specimens of Anopheles gambiae and A. funestus and the latter is considered to be the main vector, breeding in the flowing water of streams with grass margins and being both endophilic and anthropophilic. Though anopheline mosquitoes have been known to be vectors of animal virus diseases, this is the first time that they have been incriminated as the principal vector of an epidemic in Clement C. Chesterman

317. Diamino-diphenyl Sulphoxide in the Treatment of Leprosy: a Definitive Report on Expanded Trials S. G. Browne and T. F. Davey. Leprosy Review [Leprosy Rev.] 32, 194-202, July, 1961. 1 fig., 15 refs.

The expanded trials here reported of diamino-diphenyl sulphoxide (DDSO) in the treatment of leprosy were carried out in Southern Nigeria on 64 cases of lepromatous leprosy and 6 borderline, 44 tuberculoid, and 8 intermediate cases, a total of 122. The dosage resembled that of dapsone, being 100 mg. twice weekly for 3 weeks, later increased to 300 mg. twice weekly. After more than 24 months the clinical results were excellent in 23 patients, good in 65, and fair or slight in 17; treatment had to be stopped in 17 patients because of toxic effects of the drug, especially haematuria (8 cases) and dermatitis (4).

The clinical and bacteriological results were closely similar to those obtained with dapsone. As regards the toxic effects, moderately severe anaemia occurred in 2 patients, severe dermatitis in 4, a legga reaction in 14 out of 64 lepromatous patients, iritis in 2, neuritis in 24, psychosis in 3, and hepatitis in 2. There was a definite toxic effect on the kidneys, some degree of albuminuria occurring in half the patients, and in 8 cases treatment had to be discontinued because of persistent microscopic haematuria; casts also appeared in the urine in some cases. When treatment was discontinued, however, the urinary lesions gradually cleared up in all cases. It is concluded that DDSO has no therapeutic advantage over dapsone and that the toxic effect on the kidney makes its further use inadvisable. F. Hawking

318. Mycobacterial Skin Ulcers in Uganda
J. K. CLANCEY, O. G. DODGE, H. F. LUNN, and M. L. ODUORI. Lancet [Lancet] 2, 951-954, Oct. 28, 1961.
4 figs., 13 refs.

Necrotizing skin ulcers with undermined edges have been seen in 40 patients attending Mulago Hospital, Kampala; Uganda: Of these, 28 lived in a very limited area, but no reason for the high prevalence in this district was discovered. Most patients were children in good general health. Often there was a history of minor injury followed by the development, about 3 weeks later, of an indurated area covered by deeply pigmented skin which broke down to form a large ulcer. The skin around the ulcer became undermined and felt'indurated. The ulcer was usually single, but other small ulcers sometimes arose, the extensor surfaces of the arms and legs being most often affected. Healing took place slowly over 6 to 9 months, but gross deformities and contractures might develop. There were no serious systemic effects.

In 28-patients acid/alcohol-fast organisms were identified in either pus or necrotic material from the ulcers. The cultural characteristics suggested an organism resembling *Mycobacterium ulcerans* or an allied mycobacterium.

No specific remedy was found to influence the progress of the ulcers, which might require grafting. The actiology, which is obscure, is discussed.

S. T. Anning

319. Internal Intestinal Fistulae Caused by Amoebiasis: a First Report

M. DINNER and E. BADER. South African Medical Journal [S. Afr. med. J.] 35, 808-811, Sept. 30, 1961. 4 figs., 3 refs.

Although many reports on the séquelae of amoebiasis have mentioned stricture of the colon, chronic colitis, and recurrent diarrhoea as late complications of the infection the present authors could find no report in the interature of internal fistula caused by amoebiasis. From Baragwanath Hospital, Johannesburg, they therefore describe 4 such cases, 3 of them fatal, which occurred in male Africans aged 32 to 49 years. All had amoebic dysentery and 2 developed an amoeboma, which in one case was complicated by a jejuno-colic fistula while in the other the mass was removed at operation. In the remaining 2 patients perforation of the colon developed which was accompanied by peri-colic abscess formation and peritonitis.

The following factors in the pathogenesis of internal fistulae are suggested: (1) central necrosis of an amoeboma adherent to two hollow viscera, and breakdown of the abscess; (2) perforation of an amoeboma with subsequent adhesion of the small bowel to the colon; and (3) perforation followed by general peritonitis may

result in a residual abscess lying between two hollow viscera, the breakdown of this abscess subsequently resulting in the formation of a fistula. It is also suggested that the persistent diarrhoea which sometimes follows adequately treated amoebiasis may arise because of the occurrence of stricture or of the blind-loop syndrome.

R. R. Willcox

320. Eradication of Sleeping Sickness in the Sudan K. R. S. Morris. *Journal of Tropical Medicine and Hygiene [J. trop. Med. Hyg.*] 64, 217-224, Sept., 1961. 1 figs., 29 refs.

The author gives a historical account of the development of foci of Trypanosoma gamblense infection in the Southern Sudan and their eradication by chemoprophylaxis. The foci were situated on the borders with Uganda and Congo within the range of Glossina palpalis. Epidemics which occurred in these foci in 1911 were controlled by destruction of the tsetse's breeding habitat. However, the riverine vegetation subsequently regenerated and was recolonized by the fly. These localities were on the trading routes with Congo and Uganda so T. gamblense was reintroduced. The disease spread, with the number of new cases of trypanosomiasis reaching epidemic proportions by 1955. Mass treatment with pentamidine was instituted and within 5 years the number of cases had fallen from at least 272 in 1955 and 450 in 1956 to zero in 1960. R. A. Neal

321. Tris (p-aminophenyl) carbonium Salts in the Treatment of Schistosomiasis in Nyasaland

H. S. BURNETT and E. D. WAGNER. American Journal of Tropical Medicine and Hygiene [Amer. J. trop. Med. Hyg.] 10, 547-550, July, 1961. 2 refs.

Pararosaniline chloride or pararosaniline pamoate [embonate] was given to 66 patients, of whom 39 were infected with Schistosoma haematobium, 18 with S. mansoni, and 9 with both, at the Malamulo Hospital and Leprosarium, Blantyre, Nyasaland. The drugs were given by mouth, three times daily after food, in the form of sugar-coated tablets for 4 to 14 days, the dose of carbonium ion being 15 to 65 mg, per kg, body weight daily. Only 30 of the patients could be adequately followed up, these being seen at intervals for 12 weeks after treatment. The centrifuged deposit from 15 ml. of urine show and when collected is not described] was searched for schistosoma ova; while the stools were examined by a formalinether technique. Schistosomiasis is endemic in the area and therefore it was not possible to judge the curative value of the drugs.

Pararosaniline chloride suppressed egg excretion in 12 of 13 patients infected with *S. haematobium* and in one of 2 infected with *S. mansoni*. Similar results were obtained with the pamoate against *S. haematobium*, and ova disappeared from the urine for at least 6 weeks in 5 patients with infection due to *S. mansoni*. Gastrointestinal reactions, mainly nausea and vomiting, occurred in 19 of 32 patients treated with the chloride. Other transient side-effects reported by a few patients included dizziness, hallucinations, visual disturbances, and dermatitis. The pamoate, however, was well toler-

ated and side-effects occurred in only 3 of the 32 patients treated with this salt.

• The authors conclude from these results that pararosaniline pamoate is worthy of further study as a schistosomicide.

L. G. Goodwin

322. A Comparison of Bephenium Hydroxynaphthoate with Tetrachlorethylene in Hookworm Infestation

P. W. HUTTON and K. SOMERS. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med. Hyg.] 55, 431-432, Sept., 1961. 2 figs.

The treatment of 26 patients with hookworm infection and anaemia is reported from Mulago Hóspital, Kampala, Uganda. Oral and intramuscular iron, and sometimes blood transfusions, were given for the anaemia. For the hookworm disease half the patients received 5 g. of bephenium hydroxynaphthoate and the other half 5 ml. of tetrachloroethylene, each as a single dose. The drugs were given in the morning on an empty stomach; there was no preliminary fasting and no purgatives were administered. Stools were collected for 72 hours after the dose and bookworms separated in a sieve by flotation in brine. The mean number of worms collected after bephenium was taken was 218, and after tetrachloroethylene 206. On the 4th day both groups of patients were given 5 ml. of tetrachloroethylene; the mean numbers of worms collected in 72 hours from the two groups were 137 and 33 respectively. The figures suggest that more worms were left after an initial dose of bephenium than after an initial dose of tetrachloroethylene. The authors consider that bephenium gives less consistent results than tetrachloroethylene and is unlikely to replace it for the routine treatment of hookworm disease.

[No figures are given for the variance of the means and no data from which they may be calculated; the observed difference may or may not be significant.]

L. G. Goodwin

323. Filariasis Due to Brugia malayi in South Borneo (Indonesia)

A. H. KLOKKE. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med. Hyg.] 55, 433-439, Sept., 1961. 1 fig., 14 refs.

The sparse literature dealing with filariasis in Indonesian Borneo is reviewed. Malayi filariasis is endemic in South Borneo. In the Pangkoh area (southern part of Kahaian River) 2 villages (population 900) were examined, representing nearly 80% of the inhabitants. Microfilaraemia was found in 31·1% of the examined population. Nearly half of the carriers had 5 or fewer microfilariae per 20 c.mm. of blood; 10% of positive slides contained more than 50 microfilariae. Clinical disease was found in 5·2% of the population. Of the mosquitoes caught inside the houses, 95% were culicines. The bulk of these were Mansonia annulata and Mansonia longipalpis, the latter being twice as frequent as the former. A few Mansonia novochracea were also found. The small number of dissections revealed infective larvae in 3 of the 4 species of Mansonia encountered.—[Author's summary.]

Allergy

324. Immunological Studies of Ragweed-sensitive Patients Treated by a Single Repository Antigen Injection P. J. Delorme, M. Richter, S. Grant, H. Blumer, A. Leznoff, and B. Rose: Journal of Allergy [J. Allergy] 32, 409-419, Sept.-Oct., 1961. 9 figs., 18 refs.

To 35 ragweed-sensitive patients seen at the Royal Victoria Hospital, Montreal, one single injection of a repository emulsion of ragweed extract was given. Thereafter the haemagglutination titre was studied by means of the bis-diazotized benzidine technique, the skinsensitizing antibody by the Prausnitz-Küstner method, and the blocking antibody by heating the serum to 56° C. for 2 hours. In 30 of the 35 patients a significant increase in the haemagglutination titre occurred, but this showed no correlation with the skin-sensitizing and blocking antibody measurements, nor was there any relationship between clinical improvement and any of the serum activities. There was also no correlation between the clinical response and the amount of ragweed antigen administered. Adverse reactions after the injection occurred mainly in asthmatics with a high skin sensitivity and in those who had not been treated by hyposensitization methods during the previous year.

H. Herxheimer

325. Growth Rate of Children with Intractable Asthma: Observations on the Influence of the Illness and Its Therapy with Sterolds

C. J. Falliers, J. Szentivanyi, M. McBride, and S. C. Bukantz. *Journal of Allergy* [J. Allergy] 32, 420-434, Sept.-Oct., 1961. 6 figs., 19 refs.

At the Jewish National Home for Asthmatic Children, Denver, Colorado, the growth of 302 asthmatic children aged between 5 and about 17 years was observed over a period of 2½ years. On admission, 83% of these children fell below the expected mean height and body weight as well as bone age corresponding to the height. The age of onset of the asthma was not correlated with the retardation of growth, but a history of continuous administration of steroids was often elicited in those with the more retarded growth. Continuous steroid therapy affected growth adversely also during the period of observation, but brief courses of steroid therapy did not. The authors suggest that the steroids exert a growth-suppressing effect which is more marked with prednisone than with equivalent doses of cortisone.

[This is an important investigation, but the authors' suggestion is open to some doubt. Naturally, only the most severely affected patients receive continuous steroid treatment, and it cannot be decided on the basis of the present findings whether the retardation of growth is due to the severity of the asthma or to the effect of the steroids. The reported difference between the effects of cortisone and prednisone does not appear to be statistically sound.]

326. The Suprarenal Function in Allergic Asthma. Determination of the Plasma and Urinary 17-OH-Corticoids and of the Urinary 17-Ketosteroids before and after ACTH Zn

J. R. VACCAREZZA. Diseases of the Chest [Dis. Chest] 40, 121-127, Aug., 1961. 20 refs.

Tests of adrenal activity were carried out at the Faculty of Medicine, Buenos Aires, on 22 adult asthmatic patients who were all considered to have asthma of allergic origin. They were subdivided into those without symptoms (7), those with slight symptoms (10), and those with severe symptoms (5). Nine specimens of urine were first collected for 24 hours and assessed for 17-hydroxycorticoid and 17-ketosteroid content, while the plasma 17-hydroxycorticoid level was also determined. Thereafter 40 units of a slow-acting ACTH-zinc preparation was given intramuscularly and the tests repeated. None of the patients had previously received corticoid therapy.

 The excretion of 17-ketosteroids before administration of ACTH was reduced, the mean value being 9.6 mg. per 24 hours for men and 7.1 mg. per 24 hours for women, compared with normal mean values of 14 and 9 mg. per 24 hours for men and women respectively. More important was the poor response to ACTH, the average value for men remaining at 9.6 mg., while that for women rose slightly to 8.0 mg. per 24 hours. The urinary elimination of 17-OH-corticoids for both men and women was within normal limits, but showed a reduced response to ACTH, the output increasing by 123 and 167% for men and women respectively, compared with an increase of 300% in normal individuals. The values for plasma 17-OH-corticoid level were found to be increased in asthmatics (20.7 μ g. per 100 ml. in men and 26.1 μ g. per 100 ml. in women at 8 a.m., compared with 13.3 µg. per 100 ml. in 6 normal adults). The increase in the plasma 17-hydroxycorticoid level 8 hours after ACTH was also found to be diminished.

The author concludes that in patients with allergic asthma there is subclinical insufficiency of the adrenal glands and that androgenic function is more readily disturbed than is glycaemic function. The high levels of plasma 17-hydroxycorticoids may be related to the need for hydrocortisone and cortisone in response to the allergic reaction, since it was observed that the patients with fewest symptoms had the highest level of 17-hydroxycorticoids, while those with the most severe symptoms had the lowest.

[These findings confirm and extend observations of a similar nature carried out by the present author and other workers. There is accumulating evidence that some disturbance of pituitary—adrenal activity is present in asthmatics, but whether these changes are primary or secondary and how they may be related to the allergic condition is still uncertain.]

R. S. Bruce Pearson

Metabolic Disorders

327. A Long-term Study on the Use of Appetite Suppressants

W. H. LERICHE and G. E. VAN BELLE. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 673-676, Sept. 16, 1961. 3 refs.

The authors report from the University of Toronto a long-term clinical trial designed to investigate the observation that "the time span of an appetite-suppressant study considerably influences the results obtained"; the longer the study, the less effective the appetite suppressant appears to be in terms of weight reduction. Furthermore, in such a study a large number of subjects who start the clinical trial do not return after a few weeks. What are the reasons for this, and can the "success" of a clinical trial be assessed?

In the trial here described, which was "blind", 237 adult patients, mostly women, took part. Two active drugs-one an amphetamine-type drug ("biphetamine 12.5"), the other a non-amphetamine preparation ("ionamin 30")—and a placebo were used. In two 8-week periods loss of weight when biphetamine was given was 9.3 lb. (4.218 kg.) and 8.1 lb. (3.675 kg.) respectively; with ionamin it was 10.6 lb. (4.808 kg.) and 4.8 lb. (2-177 kg.). Ionamine with a daily diet of 1,000 Calories gave average weight losses of 16.2 lb. (7.350 kg.) and 4.9 lb. (2.222 kg.) respectively in the two periods. Thus the study confirmed the impression that the weight lost initially is greater than that lost later on. Of the 162 patients who did not complete the study, 69 (43%) lost at east 10 lb. (4.536 kg.) in varying periods of time. A. G. Mullins

328. Long-term Anorexigenic Therapy in Obese Diabetic Patients

B. E. HAZLETT. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 677-681, Sept. 16, 1961. 7 refs.

A long-term study of the anorexigenic agent phenmetrazine hydrochloride ("preludin"), a congener of
amphetamine, was designed to allow comparison with
short-term trials, which have been favourably reported
on. The subjects were diabetic out-patients of the
Toronto General Hospital, who were classified into 4
groups. In Group I were 29 chronically obese patients
with long-standing diabetes who had been unresponsive
to previous attempts by physician and dietitian to help
them lose weight; in Group II were 8 chronically obese
patients who had but recently been found to be diabetic;
in Group III, 20 patients who had less than 20 lb. (9 kg;
excess weight; and in Group IV, 3 young pregnant
women with maturity-onset diabetes who were overweight.

As a result of treatment patients with less than 20 lb. (9 kg.) excess weight (Group III) and patients recently found to be diabetic (Group III) had a more satisfactory reduction in weight than those who had been both dia-

betic and obese for some time (Group I). However, almost all of those who lost weight did so most effectively during the first 2 months of treatment and had almost achieved their maximum loss in 6 months. Prolongation of therapy beyond this time appeared to be of little-value. Weight-control was satisfactory in the last trimester of pregnancy in the 3 diabetics in Group IV.

Control of the diabetes generally, but not invariably, improved with reduction in weight. This was most apparent among the younger insulin-sensitive patients, in whom insulin reactions at the beginning of therapy were often a problem. Side-effects-such as skin eruption, gastro-intestinal upset, nervousness, and headache -were encountered in 25% of patients and necessitated discontinuing treatment (though often after several months) in 12.5%. Weight reduction was effected with a placebo in the 2 cases in which this was given as the initial therapy. Unusual responses were noted in 5 patients. One frankly admitted that her interest in continuing the tablets was derived from the extra "lift" and energy she attributed to them. Another lost 17 lb. (7.7 kg.) over 9 months, the loss of weight increasing in. tempo during this time: she continued to lose weight subsequently without medication and was ultimately admitted to hospital with anorexia nervosa and weighing A. G. Mullins 89 lb. (40·37 kg.).

329. Salt and Water Metabolism during Weight Reduction

P. ELSBACH and I. L. SCHWARTZ. Metabolism: Clinicaland Experimental [Metabolism] 10, 595-609, Aug. [received Oct.], 1961. 12 figs., 12 refs.

Long-term metabolic balance studies were performed on 7 severely obese patients at the Rockefeller Institute Hospital, New York, for about a year. They were given enough of a formula diet to maintain weight for the first 3 months, and then only enough to provide 600 Calories daily. Salt was added to give either a low (2 to 3 g.) or a high (10 g.) daily intake. The output of sodium was measured in the urine and stools; the weather was cool.

All the patients showed abnormalities of salt and water metabolism while on a low caloric intake, after considerable loss of weight. One was retaining sodium, but losing weight, while her daily sodium intake was 35 mEq.; when sodium intake was raised to 172 mEq. she retained 1,000 mEq. and gained 6 kg. in 14 days, but thereafter lost half the sodium and all the weight in the next 17 days. Sodium intake was then reduced to 34 mEq., and the rest of the retained sodium was lost in 17 days. Later episodes of high salt intake again caused sodium retention and weight gain, but both were slightly less when a spirolactone was added to the regimen. This patient had headaches and other symptoms and showed oedema when sodium retention was greatest. Her serum sodium concentration varied widely (up to

165 mEq. per litre) independently of other changes. Another patient likewise retained sodium and gained weight when on a high salt intake. A third was in sodium balance and losing weight on a low salt intake; when the daily intake of salt was raised to 5 g. for 35 days she stopped losing weight, but did not retain sodium; when salt intake ceased there was a very large and rapid loss of sodium and of weight. The same patient, later, was retaining sodium and not losing weight when her sodium intake was 43 mEq.; when this was raised she continued to retain sodium and at first gained, but later lost, weight. A fourth patient was retaining sodium but losing weight on a sodium intake of 50 mEq.: during a high salt intake for 30 days there were large variations in daily sodium output, but cumulative sodium balance, while her weight was increasing; sodium output remained high until the salt intake was greatly reduced, when there was a large loss of weight and lessloss of sodium. The fifth patient showed a similar, but smaller, gain in weight and retention of sodium during her period of high salt intake.

The last 2 patients were studied both before and during reduction of weight. One of them, before weight reduction, showed normally rapid changes in sodium output in response to changes in salt intake; but 7 months later, after losing 25 kg., she retained sodium and gained weight on a high salt intake. The other retained some sodium and gained some weight on a high salt intake, both before and during weight reduction.

All these obese patients, after losing weight, showed an abnormal tendency to retain sodium, and some of them were capable of retaining either sodium or water in apparently independent amounts and without the expected changes in serum sodium concentration. The authors suggest that sodium was retained in an osmotically inactive form and discuss the possible reasons. Cardiac, renal, and hepatic diseases were excluded. The effect did not depend on the nature of the diet, nor on a prolonged low salt intake; 2 control patients, who were not fat and were kept on a similar diet (in an amount sufficient to maintain weight) and with a low salt intake, G. C. R. Morris

330. Carbohydrate and Sodium Metabolism in Periodic Paralysis

P. B. DOAK and K. E. D. EYRE. British Medical Journal [Brit. med. J.] 2, 549-553, Aug. 26, 1961. 4 figs., 24 refs.

At the Public Hospital, Auckland, New Zealand, insulin sensitivity and oral and intravenous glucose tolerance tests were performed, serum electrolyte levels determined, and serial electrocardiograms (ECGs) recorded in 4 members of a family (a father and 3 children), 3 of whom suffered from periodic paralysis. In one of the children (a girl) sodium and potassium balance studies were also carried out.

While receiving a high-potassium diet one child showed a flat glucose tolerance test, but no change in the serum potassium level and no paralysis, whereas with a normal potassium intake he invariably developed paralysis and a fall in the serum potassium level. The intravenous glucose tolerance test gave a normal result during

attacks of paralysis, but there was an abnormally low rate of disappearance of glucose after the attacks. On the one occasion when this patient was tested for insulinsensitivity between attacks he showed hypoglycaemic unresponsiveness to insulin. This boy's non-identical twin sister while receiving a normal diet showed a flat glucose tolerance curve in response to 100 g. of glucose, which precipitated a severe attack; on a restricted carbohydrate diet the result of an oral glucose tolerance test (100 g. of glucose) on two occasions was diabetic in character, but a test with 70 g. of glucose gave a normal result. On all these occasions marked paralysis and a profound fall in the serum potassium level occurred. The intravenous tolerance test revealed a rapid rate of disappearance of glucose between attacks, a normal rate during attacks, and a low rate after an attack. Again hypoglycaemic unresponsiveness to insulin was demonstrated between and during attacks. Although the characteristic falls in the serum potassium level were observed both in the spontaneous and precipitated attacks, there was no exact relationship between the serum potassium level and the severity of the paralysis. ECG changes characteristic of hypokalaemia often occurred before the changes in the serum potassium level became apparent and persisted longer; this was especially seen after the intrajejunal introduction of glucose and intravenous injection of insulin. All 4 subjects, including the boy who was free from periodic paralysis, showed a high creatine and a low creatinine excretion.

The balance study on the girl showed that a change in sodium balance in either direction resulted in an increased incidence of minor attacks of paralysis, although the serum potassium level rarely fell below 3.5 mEq. per litre. The urinary potassium excretion fell during the major attacks in parallel with the fall in the serum levels. Minor attacks were usually, but not invariably, accompanied by a fall in urinary potassium excretion; on these occasions there was a close parallel between the degree of potassium retention and the serum potassium level. It is concluded that these results are consistent with the suggestion that after an attack of paralysis the peripheral uptake of glucose is reduced, owing to either exhaustion of the membrane carrier mechanism or saturation of the intracellular storage mechanisms. Rapid peripheral uptake of glucose precedes the fall in serum potassium content and is responsible, at least in part, for this fall. Changes in the intracellular content. of potassium, possibly through its binding to glycogen, take place before the changes in the serum potassium levels.

In conclusion it is suggested that the basic abnormality in periodic paralysis is a deficiency of high-energy phosphorous bonds in the muscle cells, related to an inability to store creatine. This leads to increased uptake of glucose, intracellular deposition of glycogen, hyperpolarization of the cell membrane, and a low serum potassium level, together with a deficiency of the immediate source of energy required for muscle contraction. The intermittent nature of the condition may be related to exhaustion of a carrier mechanism in the cell membrane or to a saturation storage of glycogen.

A. Gordon Beckett

Gastroenterology

331. The Rolè of the Gastrointestinal System in "Idiopathic Hypoproteinemia"

T. A. WALDMANN, J. L. STEINFELD, T. F. DUTCHER, J. D. DAVIDSON, and R. S. GORDON JR. Gastroenterology [Gastroenterology] 41, 197-207, Sept., 1961. 6 figs., 34 refs.

At the Clinical Center of the National Institutes of Health, Bethesda, Maryland, protein metabolism was studied in 18 patients with idiopathic hypercatabolic hypoalbuminaemia with oedema. When albumin labelled with ¹³¹I was administered intravenously and samples of blood, urine, and faeces subsequently collected for assay of radioactivity all the patients were found to have a low total exchangeable albumin content, a decreased ¹³¹I-albumin half-life, and an increased albumin turnover. Faecal excretion of polyvinylpyrrolidone labelled with ¹³¹I and given intravenously averaged 8.1% of the dose in 4 days compared with 0.7% in controls, suggesting that the hypoalbuminaemia was due to gastro-intestinal protein loss.

In one case the protein loss was due to acute gastroenteritis and in two others to constrictive pericarditis. In 12 of the remainder histological evidence of a lymphatic disorder of the small intestine was obtained by necropsy, laparotomy, or peroral biopsy. Most of these patients had diarrhoea or steatorthoea which did not respond to corticosteroids or gluten-free diets. The histological picture was essentially that of lymphatic dilatation. The authors propose the name "intestinal lymphangiectasia" for this condition. M. Lubran

332. Faecal P.V.P. Excretion in Hypoalbuminaemia and Gastro-intestinal Disease

A. M. DAWSON, R. WILLIAMS, and H. S. WILLIAMS. British Medical Journal [Brit. med. J.] 2, 667-670, Sept. 9, 1961. 3 figs., 15 refs.

The ¹³¹I-polyvinylpyrrolidone (PVP) test for faecal lossof protein is carried out by injecting PVP labelled with ¹³¹I intravenously in a dose of 10 to 20 μc., collecting urine and faeces separately for 4 consecutive 24-hour periods, and assaying the output of radioactivity. Thyroid uptake of iodine is blocked by the previous and conconcurrent administration of potassium iodide. Faecal excretion of ¹³¹I-PVP averages 0.52% of the dose (range <0.05 to 1.6%) in 4 days.

At the Royal Free Hospital, London, the test was carried out on 21 patients with gastro-intestinal disease, in 12 of whom the serum albumin concentration was less than 3.5 g. per 100 ml. In 11 of these the faecal ¹³¹I-PVP excretion was raised, the value being roughly inversely proportional to the serum albumin level. [However, this relationship is not as clear, from the data given, as the authors claim. See Parkins, *Lancet*, 1960, 2, 1366; *Abstr. Wld Med.*, 1961, 30, 112 for a contrary opinion.] In 3 patients with hepatic cirrhosis and 2

patients with nephrosis, all with low serum albumin levels, faecal ¹³¹I-PVP excretion was normal, suggesting that hypoproteinaemia per se does not cause increased excretion of protein. Excretion was also normal in one patient with diarrhoea and 4 patients with severe steatorrhoea; confirming that these conditions do not give rise to false positive results. The authors conclude that increased loss of protein into the gut, rather than impaired synthesis, is the important factor causing hypoalbuminaemia in gastro-intestinal disease. [It is difficult to see how this conclusion can be substantiated, as no adequate studies of albumin turnover are presented in this paper.]

333. Co⁵⁸B₁₂ Absorption (Hepatic Surface Count) after Gastrectomy, Ileal Resection, and in Coellac Disorders D. J. Fone, W. T. Cooke, M. J. Meynell, and E. L. Harris. *Gut* [*Gut*] 2, 218–224, Sept., 1961. 3 figs., 22 refs:

This paper from the General Hospital, Birmingham. demonstrates that the hepatic surface counting technique provides a satisfactory means of estimating the absorption of radioactive vitamin B₁₂ (cyanocobalamin) and describes its application in a study of vitamin-B₁₂ absorption in patients with pernicious anaemia, idiopathic steatorrhoea, and adult coeliac disease and following gastric and ileal resection. After a preliminary hepatic count of radioactivity 58Co-labelled vitamin B₁₂ was given orally (0.25 to 0.50 µg. of vitamin B₁₂ containing 0.33 to $0.50 \,\mu c$. of 58Co) and the index of absorption obtained from a second hepatic count made some time between the 6th and 10th days. Usually a single count made on the 7th day proved satisfactory. On 15 occasions parallel studies of the faccal excretion of radioactive vitamin B₁₂ were made and the results correlated satisfactorily. In 28 control subjects hepatic counts (expressed as counts per minute per 1 μc. 58Co) varied from 1,600 to 4,633 (mean 2,914, S.D. 828). The results were unaffected when the test was repeated on 6 subjects with the addition of intrinsic factor (10 mg. of intrinsic factor concentrate).

In 19 patients with pernicious anaemia values were low (0 to 720; mean 237, S.D. 231), but with the addition of intrinsic factor normal values were obtained (1,574 to 4,268). In 2 patients after total gastrectomy the hepatic count was low (0 and 66 respectively), but was restored to normal (2,365 and 2,172 respectively) by the addition of intrinsic factor. Of 24 patients after partial gastrectomy the count was normal in 18 and low (261 to 1,034) in 6. Five of these patients had clinical and haematological evidence of vitamin-B₁₂ deficiency and all 6 gave normal hepatic counts with the addition of intrinsic factor. Of 16 patients after ileal resection (for regional ileitis (14), carcinoma of the caecum (1), or ileal argentaffin tumour (1)), the count was normal in 7

and low (60 to 876) in 9. These low counts were not significantly altered by the addition of intrinsic factor. There was a general agreement between the degree of impairment of vitamin- B_{12} absorption and the amount of intestine resected.

The 50 patients with adult coeliac disease and idiopathic steatorrhoea were classified as previously described (Fone et al., Lancet, 1960, 1, 933; Abstr. Wld Med., 1960, 28, 368) according to the clinical, haematological, and jejunal histological features. Of the 22 Group-I patients with adult coeliac disease and a flat jejunal mucosa, the hepatic count was normal in 18 and low in 4. The low values were unaffected by the administration of intrinsic factor. The 28 Group-II patients with idiopathic steatorrhoea and abnormal villi (partial atrophy) could be divided into three types: (a) 8 patients who closely resembled those with adult coeliac disease except for the jejunal mucosal appearances; the hepatic count was normal in 5 and low in 3, the low values being restored to normal by intrinsic factor; (b) 7 patients with megaloblastic anaemia and low serum vitamin-B₁₂ levels. of whom 5 had a low hepatic count which became normal with the addition of intrinsic factor; and (c) 12 patients with megaloblastic anaemia, normal serum vitamin-B₁₂ levels and free gastric hydrochloric acid whose anaemia responded to folic acid; the hepatic count was normal in 11 cases and in the 12th the low level was unaffected by intrinsic factor.

The authors conclude that the test provides a useful method for the estimation of vitamin-B₁₂ absorption, since it does not require the collection of faeces or urine. The results obtained in the various disorders studied are generally in agreement with those of other workers except for those in the patients with adult coeliac disease and idiopathic steatorrhoea.

Hewett A. Ellis

334. Gastro-intestinal Cancer and Geochemistry in North Montgomeryshire

J. B. MILLAR. British Journal of Cancer [Brit. J. Cancer], 15, 175-199, June [received Aug.], 1961. 4 figs., 38 refs.

The mortality from gastric cancer has long been known to be higher in North Wales than in England. A detailed study was therefore made of cancer mortality in Llanfyllin Rural District of North Montgomeryshire, which adjoins the areas of high gastric cancer mortality and the findings related to environmental factors. (The study was later extended to include the rest of North Montgomeryshire.) The population of Llanfyllin Rural District is small and it was necessary to study a 14-year period (1946-59) to obtain useful numbers of deaths for analysis.

Altogether 75 deaths from gastric cancer and 52 from intestinal cancer were recorded. The standardized mortality ratios for the areas—based on the age distributions at the 1951 census—were: (1) for gastric cancer, male 135 and female 162; and (2) for intestinal cancer, male 143 and female 150. The high gastric cancer ratios accord with the data for the neighbouring areas, but the high ratios for intestinal cancer were unexpected as the corresponding ratios for all the rural counties of Wales were 96 (male) and 105 (femalé). No evidence was ob-

tained that the high ratios could be attributed particularly to the farming sections of the community, though there was a suggestion that gastric cancer was commoner in the rural districts of Montgomeryshire than in the small towns.

The water supplies in the Llanfyllin area are generally soft and until recently they have been mostly derived from private sources; many of them have been bacteriologically unsatisfactory. Some rocks in the area contain more than the average amount of uranium, but the amounts of uranium oxide in the drinking water are not elevated. The high rainfall in the area will result in the deposition of unusually large amounts of polonium (210Po) washed out from the atmosphere, which will be ingested by the local cattle and sheep. It is suggested that this element, derived from local meat, may be of aetiological significance.

Richard Doll

335. Recurrent Swellings of the Parotid Gland R. S. B. Pearson. Gut [Gut] 2, 210-217, Sept., 1961. 10 figs., 17 refs.

Recurrent parotid swellings are not uncommon, but their causation is not easy to determine. In a series of 104 patients showing parotid enlargement investigated at King's College Hospital, London, calculi were identified as a cause in only 14. Sialography using a watery solution of "neo-hydriol" (iodized oil) injected through a No. 22G needle gave various patterns depending upon the degree of dilatation of the main ducts or acini or of the terminal ducts, or upon the demonstration of filling defects due to calculus. Of the 104 patients studied, 61 were women and 43 men, and the main aetiological factors were thought to be (1) infection, (2) calculi, or (3) allergic. In some cases the origin was in doubt; there were 19 cases of Sjögren's syndrome, nearly all of them in women. In 16 cases there were allergic factors, and all but one had a high eosinophil count in the blood. In the infective group the organism most frequently found in the purulent secretion from the gland was Streptococcus-viridans. This group comprised 39 patients, 21 of them under the age of 20, all of whom had either normal ducts or terminal duct dilatation; of those over the age of 30, nearly all were female and most had dilated mainducts. In only 2 cases was the parotid swelling first noticed after extraction of teeth. Thomas Hunt

336. Primary Crohn's Disease of the Colon and Rectum J. S. Cornes and M. Stecher. Gut [Gut] 2, 189–201, Sept., 1961. 9 figs., 44 refs.

It has become increasingly realized that Crohn's disease is not confined to the small intestine, even though involvement of the colon was first reported in 1934. This paper records 45 cases in which Crohn's disease was confined entirely to the large intestine. Primary Crohn's disease of the colon was noted in an older age group than either regional ileitis or ulcerative colitis and was commoner in women than in men. A gradual onset with a more continuous course than in ulcerative colitis was characteristic, and perianal or rectovaginal fistulae were frequent. No definite tendency to the development of carcinoma was found, in contrast to the relatively high

incidence in ulcerative colitis—possibly because patients with Crohn's disease were operated on earlier. Widespread ulceration, pseudopolyps, dilated bowel, and perforations, which are found in some cases of ulcerative colitis, were not seen in primary Crohn's disease of the large intestine.

The paper contains a good review of the literature and emphasizes the importance of considering the diagnosis of Crohn's disease in cases of suspected ulcerative colitis, diverticulitis, or carcinoma of the colon.

Thomas Hunt

STOMACH AND DUODENUM

337. The Cardio-oesophageal Junction

J. GREENAN. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 432-439, Sept., 1961. 4 figs., 15 refs.

The mechanism of the cardio-oesophageal "sphincter" is reviewed. Reference is made to Marchand's work on the stomach of cadavers. An experiment by which the author investigated the competence of the cardio-oesophageal junction in 15 patients having a laparotomy under general anaesthesia is described. The motor nerve supply to the part was shown to be functionally intact during the experiment. Increasing the oesophageal-fundal angle, by the palpating hand of the surgeon exploring the abdomen, was shown to decrease significantly the competence of the cardio-oesophageal junction. Conversely, decreasing the oesophago-fundal angle significantly increased the competence of the cardio-oesophageal junction.—[Author's summary.]

338. The Physiology of Heartburn

S. G. TUTTLE, F. RUFIN, and A. BETTARELLO. Annals of Internal Medicine [Ann. intern. Med.] 55, 292-300, Aug., 1961. 3 figs., 12 refs.

A study of the physiology of heartburn was made on 23 patients with gastro-intestinal disease and eosophagitis at Wadsworth Hospital, Veterans Administration Center, Los Angeles, California. Heartburn was defined as a painful burning sensation located retrosternally in the midline between the xiphoid process and the manubrium. The pain moves and is characteristically wave-like; it is not oppressive like angina. In the first experiment carried out intraluminal pressures and pH were recorded in the oesophagus during the administration of 0.9% sodium chloride solution and 0.1 normal hydrochloric acid with the patients in a sitting position; in the 2nd experiment patients were placed in the supine position and asked to indicate by means of a signal marker when they experienced heartburn; and in the last experiment patients were studied repeatedly during belching.

Each of 14 men into whose stomachs both acid and saline solution had been infused developed heartburn when gastro-oesophageal reflux occurred during the administration of acid; there was no change in oesophageal motility. Heartburn during belching was transitory and was associated with well marked changes in pressure within the oesophagus. In this instance the condition appeared most likely to be related to changes in motility, for the pH was unaltered.

There would thus seem to be two mechanisms which will give rise to heartburn, but, as the authors point out, the condition is most likely to occur when oesophagitis is present. While hydrochloric acid may be a contributory cause, it is not an essential factor, as patients with achlorhydria can suffer from heartburn. It is possible that other physiological fluids, such as bile or bile acids, may also be responsible. The authors do not consider that changes in oesophageal pressure contribute much to the development of heartburn and they suggest that studies in which balloons in the distal third of the oesophagus have produced pain are not comparable in that true heartburn was not produced. However, there may be other mechanisms capable of producing heartburn which await the emergence of new techniques for their demonstration. J. S. Malpas

339. The Combined Radiologic and Gastroscopic Evaluation of Gastric Ulceration

G. D. DODD and R. S. Nelson. *Radiology* [Radiology] 77, 177-195, Aug., 1961. 12 figs., 32 refs.

The authors describe their findings in 100 patients with gastric ulceration seen at the M. D. Anderson Hospital, Houston, Texas. Gastroscopy and radiological examination were carried out in all cases, and intragastric colour photography was used wherever possible. Diagnostic criteria of malignant gastric ulceration are reviewed; the only valid sign of malignant ulceration is stated to be the demonstration of tumour in the vicinity of the crater. Nodularity of the ulcer base or margins is unreliable, as it may be due to blood clots, food particles, or benign granulation tissue. Benign ulcers are often recognized by a small line traversing the ulcer orifice, due to thin, undermined mucosa being seen in profile. Another sign of a benign ulcer is a relatively translucent band which may intervene between the niche of the ulcer and the lumen of the stomach.

An accuracy of 95% with the use of both procedures, compared with 81% and 83% respectively for gastroscopic and radiological examination alone, was recorded.

[Several excellent colour photographs are presented, and these make it apparent that intragastric colour photography considerably enhances the value of gastroscopy.]

I. McLean Baird

340. Functional Changes in the Gastro-intestinal Tract in Patients Suffering from Gastric or Duodenal Ulcer following the Administration of a Barium Meal Prepared with Cabbage Juice. (Функциональные изменения желудочно-кишечного тракта у больных язвенной болевных мелудка и луковицы двенадцатиперстной кишки после приема капустного сока (рентгенологическое исследование))

P. K. Klimov. Терапевтический Архив [Ter. Arh.] 33, 28-32, Aug., 1961. 2 figs., 7 refs.

In view of the reported beneficial effects of raw, fresh cabbage juice on gastric and duodenal ulcer, the author has investigated passage through the digestive tract of a barium meal prepared with cabbage juice instead of the usual water. Of 46 patients investigated, 15 suffered from gastric ulcer and 31 from duodenal ulcer.

The initial radiographic appearances were little different from those seen after the usual type of barium meal, but the follow-up appearances differed greatly. Generally speaking, complete evacuation of the stomach following a barium meal prepared with cabbage juice was delayed by 40 to 180 minutes. In the same way, the complete passage of the meal from the small intestine into the colon was delayed for up to 13 to 16 hours, this being accompanied by an increased tonus of the colon. In patients without gastric or duodenal ulcer and in those in the quiescent stages of ulcerative disease the radiographic follow-up appearances were the same for meals prepared with either water or cabbage juice.

A. Orlen

LIVER

341. Ammonia Tolerance as an Index of Portal-Systemic Collateral Circulation in Cirrhosis

H. O. CONN. Gastroenterology [Gastroenterology] 41, 97-106, Aug., 1961. 2 figs., 32 refs.

Even in severe hepatic cirrhosis the liver is able to metabolize large quantities of ammonia. It has been considered by many authors that a raised ammonia concentration in the peripheral blood is due to portal venous blood by-passing the hepatic parenchyma. In almost all previous studies of ammonia intolerance the ammonia level has been measured in venous blood only, but the uptake of ammonia by peripheral tissues increases as the arterial blood ammonia concentration rises, so that falsely normal venous ammonia levels may be found. In the present study, therefore, reported from Yale University School of Medicine, samples of both arterial and venous blood were withdrawn before and again 45 minutes after the oral administration of ammonium chloride in a dosage of 1 g. per 50 lb. (22.8 kg.) body weight, to a maximum dose of 3 g. The series included 10 control subjects and 50 patients with cirrhosis, in 48 of whom the diagnosis had been established by histological examination.

In the control subjects the fasting and 45-minute samples of arterial blood contained virtually the same amount of ammonia; the fasting venous samples contained slightly less ammonia than arterial blood, but the 45-minute sample contained about an equal amount. In contrast, in the cirrhotic patients the mean fasting arterial and venous ammonia levels were 137 and 122 μ g. per 100 ml. respectively (normal 111 and 101 μ g. per 100 ml.) and in the 45-minute samples they were 264 and 220 µg. per 100 ml. respectively (normal 115 and 112 μ g.). The correlation between abnormal arterial blood ammonia levels and ascites and the presence of abdominal venous collaterals and oesophageal varices was highly significant (P<0.001). There was, however, no correlation with liver size, severity of jaundice, or abnormal results in hepatic function tests, and thus a test of ammonia tolerance is not a reliable index of hepatocellular function. Of the 50 cirrhotic patients, 15 showed a normal and 35 an abnormal result in the ammonia tolerance test performed on arterial blood. The ammonia tolerance test appears, therefore, to serve

as a biochemical index of the extent of portal-systemic collateral circulation in cirrhotic patients, provided the estimations of ammonia level are carried out on arterial and not on venous blood.

W. H. Horner Andrews

342. The Demonstration of Porta-pulmonary Anastomoses in Portal Cirrhosis with the Use of Radioactive Krypton (Kr⁸⁵)

S. SHALDON, J. CAESAR, L. CHIANDUSSI, H. S. WILLIAMS, E. SHEVILLE, and S. SHERLOCK. New England Journal of Medicine [New Engl. J. Med.] 265, 410-414, Aug. 31, 1961. 6 figs., 15 refs.

The authors describe, from the Royal Free Hospital. London, their technique for the demonstration of vascular connexions between the portal and pulmonary venous systems in patients with cirrhosis. These communications have been postulated as a cause of finger. clubbing and arterial oxygen unsaturation in some cirrhotic patients. The technique is based on the fact that when a solution of radioactive krypton (85Kr) is injected into a peripheral vein 95% of the gas is expelled from the body in the expired air when the material reaches the alveoli of the lungs, so that in a normal subject less than 5% of the amount injected is found in the peripheral arterial blood because of this loss. If, however, abnormal communications exist between the portal and pulmonary venous systems then the concentration of 85Kr after its injection into the spleen will be greater in the peripheral arterial blood than it is following the injection of a similar amount into a peripheral vein, since because of the abnormal anastomosis some portal blood will have by-passed the lungs and therefore lost less of the dose of 85Kr injected.

To 12 cirrhotic patients, of whom 5 had finger clubbing but none showed cyanosis, intravenous and intrasplenic injections of 30 µc. of 85Kr were given and repeated arterial blood samples withdrawn from the femoral artery. The test revealed the presence of portalpulmonary communications in one case, which is described in detail. In discussion, the authors point out that portal venous oxygen saturation is not low enough to produce marked arterial oxygen desaturation even if the shunt were an appreciable one, so that such shunts are probably not important in producing cyanosis. Another possible cause of peripheral oxygen desaturation and cyanosis is intrapulmonary shunting due to pulmonary arterio-venous fistula, a lesion which has also been described in hepatic cirrhosis. This, besides occurring through true vascular communications in the lungs, may also be due to "functional" shunts resulting from basal lung collapse in cirrhotic patients with ascites:

A. E. Read

343. Late Results of Portacaval Anastomosis R. M. Walker, C. Shaldon, and K. D. J. Vowles. Lancet [Lancet] 2, 727-730, Sept. 30, 1961. 2 figs., 7 refs.

It has been established by the results from many centres that in patients with portal hypertension due to hepatic cirrhosis the operation of end-to-side portacaval anastomosis is the most effective procedure available to prevent haemorrhage from gastro-oesophageal varices. It has been questioned, however, whether the effect of portal-systemic venous shunt on liver function and the risk of portal-systemic encephalopathy might not outweigh the advantages of the operation.

During the past 11 years the operation of end-to-side portacaval anastomosis for portal hypertension has been the procedure of choice at the Bristol Royal Infirmary, and more than 150 of these operations have been performed. The operative technique has been described (Walker, R. M., Pathology and Management of Portal Hypertension, London, 1959). The present paper deals with the long-term results of the first 50 operations, performed between 5 and 11 years ago; the patients have been described in an initial report (Lancet, 1957, 1, 57; Abstr. Wld Med., 1957, 21, 393). Of these 50 patients, 15 have died since operation; 3 of the deaths occurred postoperatively in hospital and 12 subsequently, including 8 deaths from hepatic failure and 4 from unrelated causes. The remaining 35 patients (70%) have survived for more than 5 years, after which time no deaths have occurred; 16 of the survivors have received detailed assessment in hospital and the remaining 19 have been reviewed as out-patients.

Haemorrhage recurred in 2 of the 12 patients who died after leaving hospital; in one of these cases, in which the haemorrhage may have contributed to death, splenorenal anastomosis had been performed 2 years before portacaval shunt. Haemorrhage has recurred in only 4 of the 35 survivors, the haemorrhage being minor in 2 of these cases; in the remaining 2 cases splenectomy had been performed some time before portacaval shunt. The 12% rate of recurrence of bleeding, comprising 10 episodes in the 6 cases, contrasts strikingly with 150 episodes of bleeding in the group as a whole before operation.

Symptoms of portal-systemic encephalopathy are recurrent and severely incapacitating in 5 of the 35 survivors, and minor neuropsychiatric symptoms have occurred in another 3. The liver function of the survivors, judged clinically and biochemically, remains at about the same level as before operation; ascites, which was present at operation in 7 of the survivors, has not recurred in any case. The spleen diminished in size after operation in all cases and became impalpable in 70%; the haematological changes of hypersplenism—namely, thrombocytopenia and leucopenia—persisted after operation, but did not cause any incapacity.

Of the 35 survivors, 29 (83%) lead normal working lives, completely free from symptoms or with only minimal symptoms.

Joseph Parness

344. The Treatment of Pruritus and Hypercholesteremia of Primary Billary Cirrhosis with Cholestyramine T. B. Van Itallie, S. A. Hashim, R. S. Crampton, and D. M. Tennent. New England Journal of Medicine [New

Engl. J. Med.] 265, 469-474, Sept. 7, 1961. 2 figs., 21 refs.

Pruritus is one of the most distressing symptoms of primary biliary cirrhosis and has proved resistant to most forms of treatment. In this condition there is an accumulation of bile acids and cholesterol in the blood, probably as the result of an impaired excretion of bile acids, and it is possible that a high peripheral concentration is responsible for the pruritus. Diets containing a high proportion of unsaturated fatty acids reduce the body content of cholesterol and bile acids, as does oral administration of cholestyramine, which is a quaternary ammonium-anion exchange resin with a marked affinity for bile acids. The method of action of the diets is not known, but the resin acts by preventing reabsorption and thereby breaking the enterohepatic cycle.

There were 5 patients in the study here reported, in only one of whom was the duration of itching less than 2 years before treatment was begun. Two received the special diet with safflower or corn oil and 3 were given cholestyramine. All 5 patients experienced dramatic and long-lasting relief from pruritus within one to 3 weeks of starting treatment, the relief being complete in 3 and partial in 2. In no case was there an adverse effect on the liver. In the 4 patients in whom measurements were made there was a reduction in the serum concentrations of bile and cholic acids, especially with cholestyramine treatment, to about one-fifth of the pretreatment concentrations.

[The authors believe that, although it is not proven, bile acids and cholesterol cause pruritus. They quote other reported work in support, and it is difficult to deny that there is a strong possibility that this thesis may be correct.]

W. H. Horner Andrews

345. Manifestations of Metastatic Tumors of the Liver: a Study of Eighty-one Patients Subjected to Needle Biopsy L. F. Fenster and G. Klatskin. American Journal of Medicine [Amer. J. Med.] 31, 238-248, Aug., 1961. 21 refs.

The authors, who report from Yale University School of Medicine, New Haven, Connecticut, have analysed 81 cases of metastatic tumours of the liver studied by needle biopsy as well as by other conventional methods. The primary tumour lay in the area drained by the portal vein in 37 cases and in areas drained by systemic veins in 27 cases (the lung in 12); in 17 cases it was undetected. The clinical features are described and the importance of pain felt in the right upper quadrant as the presenting symptom is stressed. Fever was present in 19 cases and was the dominant presenting feature in 6. In 8 patients a friction rub was heard over the liver. Jaundice and ascites were common, but other clinical signs of liver disease, such as spider naevi, foetor hepatieus, and tremor, were rarely observed. The dominant physical finding was a large, firm, tender liver. Nodules could be distinguished clinically in 43 cases, and in only 4 instances was the liver impalpable. Significant leucocytosis was found in more than half the cases, but severe anaemia was rare. "Bromsulphalein" retention was abnormal in 95% of the patients tested. The serum alkaline phosphatase level was raised in 82% of those tested and was more often abnormal than was the serum bilirubin level. Needle biopsy was of great diagnostic value, and in 60 cases tumour tissue was found at the first attempt, but it was less likely to give a positive result when the liver was not much enlarged. P. C. Reynell

Cardiovascular System

346. Heart Sounds in Atrial Tumors

G. KAUFMANN, W. RUTISHAUSER, and R. HEGGLIN. American Journal of Cardiology [Amer. J. Cardiol.] 8, 350-357, Sept., 1961. 8 figs., 22 refs.

The clinical signs of the rare condition of primary tumour of the atrium are similar to those of mitral or tricuspid stenosis, except that atypical murmurs are heard which may show spontaneous variations in a short space of time or following changes in posture. In this paper an analysis of the heart sounds in 3 cases of atrial tumour, affecting the right atrium, left atrium, and both atria respectively, is presented from the University

Hospital, Zürich. In all 3 cases recordings of the phonocardiogram, electrocardiogram, and carotid pulse tracing showed that on the side of the tumour closure of the atrioventricular valve was often delayed, while closure of the semilunar valve tended to be premature, this causing abbreviation of mechanical systole of one ventricle. Since such abbreviation may also occur in severe mitral stenosis. however, this finding does not serve to differentiate the condition of left atrial tumour. The displacement of the heart sounds in atrial tumour is characteristic for the atrium affected. Thus in tumour of the left atrium either the components of the first sound are fixed or there is reverse splitting, that is, the tricuspid component precedes the mitral component, and the second sound is widely split. If the tumour is in the right atrium the first sound shows wide splitting, the closure of the tricuspid valve being delayed, while the closure of the pulmonary and aortic valves is synchronous, giving rise to a fused second sound. There is also marked exaggeration of the normal lengthening of systole on inspiration, together with considerable change on adoption of different postures. In the authors' third case, in which both atria were involved, wide splitting of the first sound and some splitting of the second sound occurred; after surgical removal of the myxoma these abnormalities disappeared. The first 2 patients died, the second suddenly from pulmonary embolism following detachment of a part of the tumour.

J. S. Malpas

347. Effect of Norepinephrine on the Phonocardiographic, Auscultatory and Hemodynamic Features of Congenital and Acquired Heart Disease

G. A. BOUSVAROS. American Journal of Cardiology [Amer. J. Cardiol.] 8, 328-340, Sept., 1961. 5 figs., '40 refs.

At Guy's Hospital, London, phonocardiographic and sphygmomanometric measurements were made on 79 patients with congenital or acquired heart disease during the intravenous infusion of noradrenaline; in 23 of these cases the haemodynamic changes resulting from the infusion were observed during cardiac catheterization.

The diagnosis of the lesion present was confirmed at operation or necropsy in two-thirds of the cases, and in the remainder after full cardiological investigation. The main side-effects of adrenaline were palpitations and a feeling of heaviness in the epigastrium and lower thorax, while headaches and dizziness were noted less frequently.

In patients with congenital heart disease the intensity. of the systolic murmur in pulmonary stenosis, the tetralogy of Fallot, and ventricular septal defect was increased by noradrenaline. In those with atrial septal defect the physical signs in uncomplicated ostium secundum were not appreciably modified, in contrast with the marked changes in ostium primum defects. In primary pulmonary hypertension and pulmonary insufficiency accentuation of the diastolic murmur was coincident with a rise in the pulmonary pressure. Diastolic murmurs appeared after the infusion of noradrenaline in patients who had undergone pulmonary valvotomy. In some cases of congenital heart disease noradrenaline was helpful in accentuating the pulmonary second sound, but the A2-P2 interval was not altered. In acquired heart disease the intensity of the systolic murmurs was increased in patients with mitral insufficiency, tricuspid insufficiency, and aortic stenosis, whereas the mid-diastolic murmurs of mitral and tricuspid stenosis were not affected. Only the early diastolic murmur of aortic regurgitation was intensified. Mitral insufficiency could not be more easily distinguished from tricuspid insufficiency by this means, nor was any help to be had in distinguishing mitral incompetence from ventricular septal defect. The haemodynamic changes resulting from the infusion were a rise in the systemic and pulmonary arterial pressure, bradycardia, abbreviation of the ventricular systole, and increased regurgitation in valvular insufficiency.

The author concludes that little help is obtained from the clinical use of noradrenaline in cardiology because of the uniform accentuation of nearly all systolic and early diastolic murmurs which occurs. However, accentuation of doubtful physical signs may be helpful, and the finding on cardiac catheterization of a simultaneous rise in the systemic and pulmonary pressures indicating the presence of a shunt may help to distinguish Fallot's tetralogy from pure pulmonary stenosis.

J. S., Malpas

348. Hemodynamic Effects of Amyl Nitrite and Phenylephrine on the Normal Human Circulation and Their Relation to Changes in Cardiac Murmurs

W. Beck, V. Schrife, L. Vogelpoel, M. Nellen, and A. Swanepoel. *American Journal of Cardiology [Amer. J. Cardiol.*] 8, 341–349, Sept., 1961. 8 figs., 17 refs.

This communication from Groote Schuur Hospital (University of Cape Town), South Africa, describes the effect of amyl nitrite and phenylephrine on the blood pressure, cardiac output, and phonocardiographic findings in 13 patients without haemodynamic abnormality

or only mild pulmonary stenosis who were studied during cardiac catheterization. Previous work is reviewed and a full account of the methods used is given. Because the effect of both drugs is transitory the Fick and ballistocardiographic methods for determining cardiac output are unsatisfactory and the authors therefore used the dye dilution method, with indocyanine green as the dye, for estimation of cardiac output.

Amyl nitrite produced a pronounced fall in the systemic blood pressure, but had little effect on right ventricular or pulmonary arterial pressures. Cardiac output increased as a result of the tachycardia due to inhibition of the carotid sinus and aortic baroceptors, but the stroke volume remained unchanged. The striking increase in right ventricular pressure following inhalation of amyl nitrite in the presence of pulmonary stenosis could be explained orly by an increase in venous return, for which additional evidence was the finding of a shortened circulation time and increased forward flow. The fall in systemic pressure would explain why ejection murmurs are increased, whereas left-sided regurgitant murmurs diminish.

Phenylephrine produced a marked change in the pressure gradient between the systemic and the pulmonary circulations and also between the systemic circuit and low pressure areas of the heart. This would explain the increase in the intensity of left-sided regurgitation murmurs and the murmur of Fallot's tetralogy. The unpredictable effect on ejection murmurs is attributed to the variable response by the stroke volume. It was noted that the cardiac output was always decreased by phenylephrine.

J. S. Malpas

349. Systemic and Pulmonary Emboli before and after Mitral Commissurotomy

F. Kelloge, Chi Kong Liu, I. W. Fishman, and R. Larson. *Circulation* [Circulation] 24, 263–266, Aug., 1961. 16 refs.

Systemic and pulmonary emboli are frequent and serious complications in mitral stenosis. The authors report that of 149 patients who underwent mitral valvotomy at two hospitals in Los Angeles, 42 had had 62 systemic emboli before operation, 9 had emboli during operation (4' dying), 17 had 21 systemic emboli after operation, 12 for the first time, while 4 patients died from late cerebral embolism. It is noted that 13 of the preoperative and 5 of the postoperative embolic incidents occurred in patients in normal cardiac rhythm, but the incidence was much higher in those with atrial fibrillation. In most of the patients with postoperative embolism the valyotomy was considered to have been adequate. Of 32 patients in whom atrial thrombus was found at operation, 9 had had emboli before operation and 4 had embolism during or after it; so that the incidence of embolism was not increased. Calcification of the valve also appeared to be irrelevant. Of the 20 patients who suffered pulmonary embolism, 10 before operation and 10 after it, 4 died.

The incidence of systemic embolism after operation was less than before it, but as in several patients single incidents had occurred many years previously, the preoperative incidence per annum per patient appeared in this series to have been less than the postoperative incidence. It is concluded that valvotomy does not prevent or decrease the incidence of embolism and that prolonged anticoagulant therapy is more effective.

[As the authors acknowledge, other workers have found a markedly reduced incidence of embolism after operation, and this too is the conclusion usually accepted in Great Britain.]

M. Meredith Brown

350. The Persistence of High Body Sodium in Previously Edematous Patients with Heart Disease

H. J. CARROLL and S. J. FARBER. Circulation [Circulation] 24, 626-632, Sept., 1961. 17 refs.

Measurements of body weight, total body water, and total exchangeable sodium (T.E.Na) were made at Bellevue Hospital, New York, in 18 patients with congestive heart failure after their weight had become stable following the loss of oedema with conventional treatment and compared with those in a control group of 27 hospital patients with no evidence of heart disease. Total body water was determined by an antipyrine dilution technique and T.E.Na by a radioactive sodium dilution technique.

Total body water averaged 52.2% of body weight in both groups. Mean T.E.Na was 3,140 mEq. in the cardiac group and 2,896 mEq. in the control group, but the mean body weight was 6.0 kg. less in the cardiac group. When comparison was made between the cardiac group and a control group of equal mean body weight the difference in T.E.Na was 510 mEq. (the control group having the lower value). There would therefore appear to be a significantly larger amount of sodium stored in the bodies of compensated cardiac patients, possibly in an osmotically inactive form bound to chondroitin sulphate in connective tissue. Serial studies in 7 of the cardiac patients showed that a fall in T.E.Na. occurred in 3 of them over several months without any loss of body weight or of total body water, but the other 4 did not lose their excess sodium. K. G. Lowe

DIAGNOSTIC METHODS

351. The Application of the Thermal Injection Method in the Diagnosis of Heart Disease. (Die Anwendung der Thermoinjektionsmethode in der Diagnostik der Herzfehler)

H. Kreuzer, B. Bostroem, and F. Loogen. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 86, 1761-1766, Sept. 15, 1961. 11 figs., 7 refs.

In an attempt to improve the value of pressure measurements and blood gas analysis in the diagnosis of heart disease the authors, working at the Medical Academy, Düsseldorf, have elaborated an injection method with cold as an indicator. It is performed as follows: 2 to 5 ml. of physiological saline at 0° C. is injected into the heart by a syringe with double walls (to prevent heat absorption from the operator's hands) to which is attached a catheter, in the closed end of which there are minute, radiating openings. To measure the temperature

of arterial blood a thermistor is mounted at the tip of a cannula and for venous blood it is incorporated in the. end of the usual cardiac catheter. These measurements of temperature are recorded as a time-temperature curve by a direct-writing apparatus connected to the thermistors. For investigation of a left-to-right shunt the best results are obtained when cold saline is injected into the pulmonary aftery and the thermistor lies as close as possible to the cardiac defect. For investigation of a right-to-left shunt and for estimation of cardiac output cold saline is injected into a venous portion of the heart and the thermistor inserted in the femoral artery. The special value of this method is said to be that it detects blood shunts too small to be recognized by blood gas analysis and that cardiac defects, especially those in uncommon situations, can be located with precision. Further, from the positioning of the thermistor the direction of the blood flow can be ascertained and thus the presence of regurgitation from minor degrees of valvular incompetence detected. The authors claim the practical 'value of the method to lie (1) in the great assistance it gives in making a differential diagnosis in difficult cases; (2) in helping the surgeon to determine his technique for dealing with cardiac defects when, in addition, very small shunts are present or they are of an uncommon kind; (3) in providing a sufficiently accurate estimate of cardiac output and of circulation time: (4) in the investigation of infants, since no loss of blood is entailed: (5) in its freedom from all toxic and untoward effects, so that it can be repeated in patients in whom optimum certainty of the results likely to be obtained is essential; and (6) in the cheapness of the initial outlay for the apparatus and its low running costs.

. E. S. Wyder

352. The Phonocardiogram and Electrocardiogram as Indicators of the Severity of Congenital Pulmonary Stenosis: Pre- and Postoperative Studies of 19 Cases. [In English]

B. LANDTMAN, E. Weis, and I. KANTERO. Annales paediatriae Fenniae [Ann. Paediat. Fenn.] 7, 169–188, 1961. 3 figs., 27 refs.

At the Children's Hospital, University of Helsinki, 19 patients ranging in age from 6 to 18 years with pure congenital pulmonary stenosis were studied before and after operation by phono- and electrocardiographic methods in order to determine the preoperative degree of stenosis and the subsequent effects of valvotomy. By these two methods it was possible to estimate the amount of right ventricular hypertrophy and to correlate this with right ventricular pressures obtained by cardiac catheterization. Although catheterization was carried out on all the patients before operation, it was, for various reasons, performed on only 12 of them postoperatively. The valvotomy was by the transarterial route in 12 cases, but in the remaining 7 under direct vision with the aid of hypothermia.

After valvotomy the phono- and electrocardiograms showed regression of the signs of pulmonary stenosis in 14 of the patients. The diminished load on the right ventricle was frequently recorded earlier in the phonogram than in the electrocardiogram; thus 6 patients

showed definite improvement in the phonogram 2 weeks after operation without a corresponding improvement in the electrocardiogram. Detailed evidence is presented to show that recording of both the phonocardiogram and electrocardiogram provides a useful means of evaluating the severity of congenital pulmonary stenosis and of the operative results. While maximum information is best obtained by the use of both procedures, nevertheless long-term serial observations are often required. Serial phono- and electrocardiograms also offer a means of selecting those patients who, after valvotomy, will require further studies and eventually a second operation.

P. T. O'Farrell

353. Cardiographic Patterns in Systolic and Diastolic Overload of the Left Ventricle

L. SEDZIWY and J. SHILLINGFORD. British Heart Journal [Brit. Heart J.] 23, 533-538, Sept., 1961. 5 figs., 9 refs.

In this paper doubt is thrown on the diagnostic significance of the theory advanced by Cabrera and Monroy (Amer. Heart J., 1952, 43, 661; Abstr. Wld Med., 1952, 12, 521) that the effect of diastolic overload of the left ventricle, such as occurs in mitral or aortic regurgitation. would have a different effect on the cardiogram from that produced by systolic overloading as in hypertension and aortic stenosis. The authors' doubts are based on their findings in a small series of 11 cases, investigated at the Postgraduate Medical School of London, in which they found considerable overlap in the cardiographic patterns in the two groups. They admit that a statistical survey of a larger number of cases might well show, on average, essential differences between the two groups, but, they conclude, "in our small series we have found enough evidence to cause us to have doubts about its diagnostic William A. R. Thomson significance".

354. The Exercise Electrocardiogram in Patients with Cardiac Pain

H. G. LLOYD-THOMAS. British Heart Journal [Brit. Heart J.] 23, 561-577, Sept., 1961. 21 figs., 42 refs.

At the London Hospital the author studied the electrocardiogram after exercise in 187 patients aged 30 to 79 years with "classical cardiac pain" using the three standard leads, Lead IIIR, and the chest leads CR1, CR4, and CR7. It was found that the most valid indication of myocardial ischaemia at the time of exercise or shortly after is the S-T segment that shows a plane (that is, a segment which is flat for a measured 0.1 second or longer) or a sagging deformity (that is, a segment that at some inferval during its course shows a decline from the level of the J). It is stressed that the development of this change may be delayed and only become apparent 4 minutes or more after the exercise has been completed. Other changes may occur after exercise that are not seen in healthy subjects-for example, depression of T-U, inversion of U, dwarfing of R in CR4, elevation of S-T, development of tall T waves and of the S2S3 pattern—but these are usually accompanied by the ischaemic deformities of the S-T segment.

[This is an article which should be read in full. It not only provides fresh information on an important subject, it also provides one of the most balanced and practical reviews of the subject that has appeared for a long time—and in a commendably short space.]

William A. R. Thomson

CONGENITAL HEART DISEASE

355. A Comparison of the Pulmonary Blood Flow between Left and Right Lungs in Normal Subjects and Patients with Congenital Heart Disease

C. T. DOLLERY, J. B. WEST, D. E. L. WILCKEN, and P. HUGH-JONES. Circulation [Circulation] 24, 617-625, Sept., 1961. 3 figs., 7 refs.

In this study of regional pulmonary blood flow carried out at Hammersmith Hospital (Postgraduate Medical School of London), the subjects inhaled a known volume of air containing a minute amount of carbon dioxide labelled with radioactive oxygen (half-life 2 minutes) and then held their breath for about 10 seconds while gamma-ray emission was measured by two pairs of crystal scintillation counters arranged in front of and behind each lung. The rate of fall in the counting rate during the apnoeic period was taken as a measure of blood flow through the lung tissue lying between the pairs of counters.

In 6 young healthy subjects there was a significantly higher blood flow in the left pulmonary upper zone than. in the right upper zone. In 7 patients with isolated pulmonary stenosis and 7 with Fallot's tetralogy there was an even more marked increase in flow in the left upper zone than the right. The mean flow rates were notsignificantly different from normal in the patients with pulmonary stenosis, but were low in those with Fallot's tetralogy. It is suggested that the predominant flow to the left upper zone might be explained by the direction of flow and kinetic energy of the blood in the main pulmonary artery and that such an effect would be increased by the jet flow in pulmonary valvular stenosis. Patients with ventricular septal defect and patent ductus arteriosus had equal flow rates through the right and left upper zones, but in those with atrial septal defect the right upper zone had a slightly higher flow than the left. The detailed results are tabulated. K. G. Lowe

356. Factors in the Aetiology of Atrial Septal Defect M. CAMPBELL and P. E. POLANI. British Heart Journal [Brit. Heart J.] 23, 477-493, Sept., 1961. 1 fig., 26 refs.

We have made enquiries about the families of 170 patients with atrial septal defect for genetic or environmental factors that might help to explain its aetiology. Many of our patients (16%) had also other malformations of the hear, but generally these were less important. Some had non-cardiac malformations as well.

A congenital malformation of the heart, most often an atrial septal defect, was found more often than would be expected by chance in the sibs of our propositi with atrial septal defect $(1 \cdot 1\%)$ and in their parents $(1 \cdot 3\%)$. Many sibs, perhaps more than would be expected, had also non-cardiac malformations $(2 \cdot 1\%)$. The parents

of the propositi were first cousins more often than would be expected (1.9%). This suggests that some of the cases are due to recessive Mendelian inheritance. When 2 members of a family each have an atrial septal defect, they are most likely to be a parent and child or 2 sibs. In some families there is good evidence of dominant Mendelian inheritance with incomplete penetrance. We think that these two mechanisms could explain only a proportion of cases and that environmental factors also are of importance.

Mean paternal age exceeded mean maternal age by 3 03 years, which is more than the normal difference (2 3 years) and may point to a genetic error, at least in some cases. Neither maternal age nor birth order were proved to have any effect on the incidence of atrial septal defect, but there were several first-born children or mothers of 35 and over and we think this is worth further investigation.

As in most reported series, there were more girls and women than boys and men, the ratio being 1.7:1. The sex incidence was more nearly equal in the first decade, but the reason for this is not clear. Both boys and girls with atrial septal defect were a little lighter at birth than their normal sibs, particularly the boys. More boys with atrial septal defect were born in January and February and the excess was enough to make the births in the first quarter about double the births in the other three quarters. There was no difference in the quarterly incidence of births for the girls.—[Authors' summary.]

357. The Reopened Ventricular Septal Defect: a Syndrome following Unsuccessful Closure of Interventricular Septal Defects Particularly in Association with Infundibular Stenosis

H. W. MARCH, F. GERBODE, and H. N. HULTGREN. Circulation [Circulation] 24, 250-262, Aug., 1961. 5 figs., 17 refs.

From the Presbyterian Medical Center, San Francisco, 7 cases are described in detail in which operative closure of a ventricular septal defect was unsuccessful. being followed by persistence or recurrence of the left-toright shunt. In 6 of these patients there was associated infundibular stenosis, which was relieved at operation. Most of them had some disability before surgery, but none had been in heart failure. The defects were in the membranous septum and were repaired by suture and application of an "ivalon" patch after arrest of the heart with potassium. Findings suggestive of a persistent shunt appeared within a few days of operation. There was a grave deterioration in the patient's condition, with tachycardia, dyspnoea, a systolic murmur and thrill. followed by heart failure; several patients showed pulmonary insufficiency and 3 had tricuspid incompetence. Radiography revealed cardiac enlargement, hilar engorgement, and pulmonary congestion. Some of the patients developed bundle-branch block. Cardiac catheterization confirmed the reappearance of the shunt, which was often greater than before operation, with strikingly increased pulmonary flow and elimination of the infundibular gradient. In all cases a second operation was performed, when the prosthesis was found to be

detached and often fractured. Two of the patients died but in the remaining 5 the defect has remained closed.

In view of this experience the authors have abandoned potassium arrest of the heart and use instead general body hypothermia with extracorporeal circulation, while the defect is now sutured directly with silk and reinforced with a crimped "dacron" patch. With this technique there have been no further cases of persistent or recurrent shunt. The profound circulatory disturbance after failed operation is attributed not only to the relief of infundibular obstruction, but also to the operative trauma received by the heart from potassium arrest and extensive ventriculotomy.

M. Meredith Brown

358. Corrected Transposition of the Great Vessels W. Beck, V. Schrire, L. Vogelpoel, M. Nellen, and A. Swanepoel. *British Heart Journal [Brit. Heart J.]* 23, 497-511, Sept., 1961. 9 figs., 23 refs.

The authors describe 5 cases of corrected transposition of the great vessels seen at Groote Schuur Hospital, University of Cape Town. They define the condition as one in which there is transposition and inversion of these vessels accompanied by inversion of the ventricles, the atria and their venous connexions being normal. The right atrium connects with a structurally left ventricle through a bicuspid valve and this ventricle connects with a pulmonary trunk which is posterior and to the right of the aorta. The left atrium connects with a structurally right ventricle through a tricuspid valve and empties into an aorta anterior and to the left of the pulmonary trunk. The great vessels pass upwards side by side without crossing, so that oxygenated blood reaches the aorta and deoxygenated blood the pulmonary artery. In addition the coronary arteries are also transposed and inverted. The circulation is therefore functionally normal and the condition difficult to diagnose in the absence of other abnormalities which may lead to investigation.

Since the atrio-ventricular bundle passes along the septal wall of the right-sided ventricle conduction defects are common and may suggest the diagnosis. The latter may also be suggested by the observation that a split basal second sound is heard better on the right side than on the left, or a louder second sound on the left than on the right, though this is generally misinterpreted as being due to pulmonary hypertension. Radiologically, the antero-posterior radiograph may show a convexity in the upper left border of the heart normally occupied by the pulmonary artery, but in cases of transposition this is due to the anterior and left position of the ascending aorta. The midline and posterior position of the pulmonary trunk may indent the barium-filled oesophagus. During cardiac catheterization difficulty may be experienced in entering the pulmonary artery since the rightsided atrio-ventricular valve lies so close to the pulmonary valve, a condition normally applying to the mitral and aortic valves. A lateral film, however, will clearly show that the pulmonary trunk is lying far posterior to the anterior cardiac border and will thus establish the diagnosis. The abnormality is best demonstrated by angiography, which shows the posterior and midline position of the pulmonary trunk and the ascending aorta passing up the left border of the heart. Corrected transposition is usually accompanied by other cardiovascular defects, which can be diagnosed in the usual manner by cardiac catheterization or angiography.

The authors describe the clinical findings and results of investigation in 5 cases—3 with a ventricular septal defect, one with the pentalogy of Fallot, and one with situs inversus. The difficulty of clinical diagnosis is illustrated by the fact that in only one of these cases was corrected transposition suspected before operation or investigation. They emphasize the ease with which the ventricular septal defect can be approached in the absence of the normal crista supraventricularis of the right ventricle and the difficulty of approach to the left-sided tricuspid valve, which is often incompetent.

H. G. Farquhar

DISTURBANCES OF RHYTHM AND CONDUCTION

359. Ventricular Premature Beats Diagnostic of Myocardial Disease

L. A. SOLOFF. American Journal of the Medical Sciences. [Amer. J. med. Sci.] 242, 315-319, Sept., 1961. 1 fig., 16 refs.

In this electrocardiographic (ECG) study, undertaken. to determine the relationship of the contour of premature ventricular beats, the commonest cardiac arrhythmia in man, to the presence or absence of underlying heart disease 4,000 consecutive patients entering Temple University Hospital, Philadelphia, were examined, among whom 411 instances of ventricular premature beats were found. These 411 patients were divided into two groups: (1) those with the classic ECG pattern and (2) those with a bizarre ECG pattern. Of the 169 patients in Group 1, 71 had otherwise normal hearts and 98 had clinical and other evidence of myocardial disease, whereas of the 242 patients in Group 2, all had clinical, radiological, or ECG evidence of myocardial disease. The various bizarre contours of the premature ventricular beats are discussed and illustrated in the text. It is concluded that this study strongly suggests that bizarre premature ventricular beats characterized by abnormalities in depolarization, repolarization, or both, are évidence of underlying myocardial disease; the author considers that vectorcardiographic analysis of these premature beats might be even more discriminatory and diagnostic. P. T. O'Farrell

360. Prevention of Stokes-Adams Seizures with Chloro-thiazide

L. TOBIAN. New England Journal of Medicine [New Engl. J. Med.] 265, 623-628, Sept. 28, 1961. 7 figs., 8 refs.

The author reports from the University of Minnesota Hospitals, Minneapolis, the effect of chlorothiazide on 10 patients suffering from Stokes-Adams seizures. (The paper is largely taken up by the 10 detailed case reports.) In 8 of the patients with a fairly long history of seizures the administration of chlorothiazide in a dosage sufficient to lower the plasma potassium level by

at least 0.6 to 1.1 mEq. per litre largely abolished the seizures. The optimum results occurred when the plasma potassium level had been reduced to between 3.5 and 3.9 mEq. per litre. In all 8 cases some atrio-ventricular conduction was present. In 2 patients there was a distinct improvement in cardiac conduction, and in one of these a change from complete heart block to normal sinus rhythm was achieved. In 4 patients the drug prevented syncope, though the 2:1 atrio-ventricular block persisted. The lessened incidence of seizures was not accompanied by any significant change in the pH of the plasma.

In the 9th patient the plasma potassium level was not lowered sufficiently and treatment with chlorothiazide had no effect on the frequency of seizures. The 10th patient continued to have complete atrio-ventricular block throughout the course of treatment and the effect of chlorothiazide on the frequency of seizures was therefore difficult to assess with certainty.

R. Wyburn-Mason

CORONARY DISEASE AND MYOCARDIAL INFARCTION

361. The Effect of Vitamin A and Vitamin D Capsules upon the Incidence of Coronary Heart Disease and Blood Cholesterol

F. C. H. Ross and A. H. CAMPBELL. Medical Journal of Australia [Med. J. Aust.] 2, 307-311, Aug. 19, 1961. 19 refs.

For several years it was customary in the Repatriation Chest Clinic, Caulfield, Victoria, to administer to patients with "subnormal health" a capsule containing 6,000 units of vitamin A and 1,000 units of vitamin D 3 times a day, and advantage has been taken of this circumstance to examine the long-term effect of this preparation on the incidence of coronary disease.

In this retrospective study 136 male patients so treated who were at least 45 years old in January, 1955, and 271 untreated control patients were followed up until death or until June 30th, 1960. The only criterion for allocation to the former group was that during the time of observation the patient had received the vitamin capsules for at least 6 months, but the majority of the group had taken the capsules for 2 to 5 years. [No further details are available about the duration of administration.] Any evidence of coronary heart disease was followed up retrospectively, and electrocardiograms were available for this study. The following criteria for coronary heart disease were accepted: myocardial infarction reported by an independent cardiologist; post-mortem evidence of myocardial infarction; sudden death certified by the attending practitioner as due to coronary heart disease; or typical or profracted angina, with or without electrocardiographic changes. Of the treated group, 8 (5.8%) had developed coronary heart disease at the end of 5½ years of observation compared with 43 (15.8%) of the control group. Moreover, the incidence of cerebrovascular accidents and even that of malignant disease was substantially higher in the control than in the treated group.

The effect of the vitamin capsules upon the serum cholesterol level was examined in 20 males between the ages of 37 and 72 years, 13 of whom were patients and 7 members of the staff. No effect was observed on subjects with an initial serum cholesterol level below 250 mg. per 100 ml., but when the initial level was above this figure it was reduced by a mean of 30 mg. per 100 ml. after the administration of 3 vitamin capsules a day for 2 to 4 weeks.

There is independent evidence that vitamin A influences cholesterol metabolism and has a protective effect on experimental atherosclerosis in hens. The authors discuss the available literature and suggest that a relative vitamin-A deficiency might have been an important factor in the production of coronary heart disease in the control group.

[In view of the expensive and time-consuming investigations in progress for the elucidation of the mechanism of coronary heart disease it would be perhaps worth while to carry out a controlled experiment in order to confirm or refute the suggestions implied in this paper.]

Z. A. Leitner

362. Influence of Reduction of Serum Lipids on Prognosis of Coronary Heart-disease: a Five-year Study Using Oestrogen

M. F. OLIVER and G. S. BOYD. Lancet [Lancet] 2, 499-505, Sept. 2, 1961. 2 figs., 38 refs.

A study of the effect of reducing the serum lipid levels on the prognosis in coronary heart disease is reported from the Royal Infirmary, Edinburgh. From among 182 patients aged 35 to 64 admitted to the hospital within 48 hours of the first attack of acute myocardial infarction 100 were selected for inclusion in the trial, 50 serving as a control group and 50 receiving ethinyl oestradiol in a dosage of 200 μ g. daily. A substantial reduction in the serum cholesterol levels in the treated group was maintained over a period of 5 years. In all except 2 patients gynaecomastia developed and although the majority tolerated the dosage satisfactorily, it was reduced after 2 years in 4 cases to 150 µg. daily. In one patient a breast abscess developed. Assessment of the results at the end of 5 years showed that 24 patients in the control group and 22 patients in the oestrogen-treated group had had further episodes of coronary infarction, with 6 deaths in the control group and 4 in the treated group.

The authors conclude that reducing the serum cholesterollevel over prolonged periods does not alter the prognosis in coronary heart disease once coronary infarction has occurred.

J. Robertson Sinton

363. Smoking Habits and Coronary Atherosclerotic Heart Disease

D. M. SPAIN and D. J. NATHAN. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 683-688, Sept. 9, 1961. 18 refs.

The association, if any, between smoking habits and the incidence of coronary disease was studied over a 3year period at Beth-El Hospital, New York, in 3,000 male members of a Jewish organization. Each individual was subjected to a full medical examination and on the information obtained at an interview about their smoking habits they were divided into 4 main groups: (1) non-smokers, (2) less than 40 cigarettes a day, (3) over 40 cigarettes a day, and (4) cigars and/or pipes. Statistical analysis showed that the incidence of atherosclerotic heart disease (angina pectoris, coronary insufficiency, and infarction) was higher in heavy smokers (over 40 cigarettes a day) than in the other groups, this association being more significant in males under the age of 51 years. It was also noted that serum cholesterol levels of over 300 mg. per 100 ml. were more frequently observed in heavy smokers than in the others, particularly men whose dietary intake of saturated animal fat was high.

Since many factors have a bearing on atherogenesis it was not possible to establish an actual causal relationship between smoking and atherosclerosis. The authors state, however, that there was suggestive evidence that cigarette smoking may play a part in the precipitation of acute myocardial infarction in individuals who already have advanced coronary atherosclerosis. No positive association was observed between cigar smoking, pipe smoking, or a history of previous smoking and the incidence of coronary atherosclerotic heart disease. Further, the findings have no bearing on the effect of smoking in individuals with established clinical coronary heart disease.

P. T. O'Farrell.

364. Tobacco Smoking and Serum Lipids in Old Men R. M. Acheson and W. J. E. Jessop. *British Medical Journal [Brit. med. J.]* 2, 1108–1111, Oct. 28, 1961. 2 figs., 17 refs.

The interrelationships between coronary heart disease, the serum lipid levels, and tobacco smoking were studied in 221 males over the age of 65, all of whom were pensioners of an industrial concern in Dublin. The authors point out that a definite relationship has already been established between cigarette smoking and cardiac infarction in younger subjects, but no reported series has included enough patients over the age of 65 to permit definite conclusions to be drawn. In the present investigation special attention was paid to the clinical status of the subjects, the serum lipid levels, tobacco consumption, and dietary intake.

It was found that smoking in men aged 65 to 85 years, whether of pipes or of cigarettes, was not associated with an increased serum cholesterol level or a raised β : α lipoprotein ratio. The significance of this finding is discussed. [This succinct and valuable paper should be studied in the original by all those interested in this subject.]

P. D. Bedford

365. Lipaemia and Blood-coagulation Defects in Relation to Ischaemic Heart-disease

D. C. O. James, J. Drysdale, J. D. Billimoria, D. Wheatley, C. J. Gavey, and N. F. Maclagan. *Lancet [Lancet]* 2, 798-802, Oct. 7, 1961. 5 figs., 27 refs.

The relationship between the degree of lipaemia and the coagulation and fibrinolytic properties of the plasma in normal subjects as compared with patients with ischaemic heart disease has been further studied at the Westminster Hospital, London. Lipaemia, as turbidity, was measured by nephelometry, plasma coagulation by the "stypven" clotting time, and fibrinolysis by estimating the "50% lysis time" of whole blood.

Two hours after a fat-free breakfast the degree of lipaemia was significantly greater and the stypyen time significantly shorter in patients with angina (24 cases). or myocardial infarction (37) than in 31 normal control subjects, and these indices did not depend upon age: Compared with normal subjects, patients with angina had a longer 50% lysis time, but not patients with myocardial infarction. Again, after a breakfast which contained 42 g. of butter the lipaemia in normal subjects was greater and the clotting time shorter at 2 hours than at 4 hours. but the lysis time was prolonged only at 4 hours. In patients with angina the lipaemia was maximum at 4 hours, but the greatest shortening of the clotting time and lengthening of the 50% lysis time occurred at 2 hours. Similar results were obtained in patients with myocardial infarction, but the clotting time was shortened only a little. The stypven clotting time showed a rough correlation with the degree of lipacmia, but the fibrinolytic activity showed no such trend.

Since some of these findings do not allow neat correlations to be made, the only conclusion reached is that in a proportion of patients with ischaemic heart disease there is a significant abnormality of lipid metabolism which has some effect on blood coagulation and fibrinolysis.

T. B. Begg

366. Epidemiology of Ischemic Heart Disease among White Males. I. Relationship between Coronary Atherosclerosis and Cancer of Various Sites.

H. M. PARRISH. Journal of Chronic Diseases' [J. chron. Dis.] 14, 311-325, Sept., 1961. 27 refs.

This investigation was based on a study of the case records of 2,731 white male patients aged 40 years or more who came to necropsy at the Grace-New Haven Community Hospital, Connecticut, during the years 1935 to 1955. A distribution of the causes of death into five disease groups was made as follows: (1) cancer of various sites; (2) accidental causes; (3) diabetes mellitus; (4) ischaemic heart disease; and (5) all other causes. Group 4 (ischaemic heart disease) included any patient in whom one or more of the following conditions was listed as a finding at death: coronary thrombosis, coronary arterial occlusion, coronary occlusion due to atherosclerosis, myocardial infarction, angina pectoris, and coronary insufficiency; when diabetes and cancer coexisted the subject was allocated to Group 5, but when ischaemic heart disease was found in a patient dying with diabetes, cancer, or accidentally the case was allocated to the appropriate Group 1, 2, or 3. In assessing the degree of coronary arterial blockage, obstruction due to atherosclerosis was distinguished from obstruction. due to clot. On the basis of the description of the macroscopic appearances, which was considered to be sufficiently accurate and detailed, five grades of atherosclerotic blockage were recognized: (1) no evidence of atherosclerosis; (2) narrowing of the vessel lumen by from 1 to 49%; (3) narrowing of the lumen by 50 to 89%; (4)

narrowing by 90 to 99%; and (5) complete obstruction by the atherosclerosis.

The records of 132 patients with lung cancer were compared with those of 132 accident victims, the two groups being matched in regard to age, race, body weight, and presence of hypertension or of other diseases known to influence the development of atherosclerosis. No significant difference between the groups in respect of degree of coronary arterial blockage, either from atherosclerosis or from clot, was found. Comparisons were also made between groups of patients with cancer at 10 different sites, with similar results; furthermore, when the combined cancer group was compared with the combined accident group no significant difference could be established. A comparison of the combined cancer group with all other groups in the necropsy population revealed that more severe coronary obstruction was present in the latter. This "control" group, however, was shown to be heavily weighted by patients with atherosclerotic conditions, including ischaemic heart disease, diabetes mellitus, and hypertension. A control group composed of subjects dying from accident was therefore considered to be more representative of the general population; but from this comparison it was concluded that no association existed, either positive or negative, between cancer and coronary arterial obstruction due either to atherosclerosis or to clot. Eirlan Williams

367. Epidemiology of Ischemic Heart Disease among White Males. II. Autopsy Incidence of Ischemic Heart Disease and Autopsy Prevalence of Coronary Atherosclerosis

H. M. PARRISH. Journal of Chronic Diseases [J. chron. Dis.] 14, 326-338, Sept., 1961. 1 fig., 26 refs.

On the basis of the necropsy records used in his previous investigation [see Abstract 366] the author has calculated the necropsy incidence of ischaemic heart disease during the four periods 1935-9, 1940-44, 1945-9, and 1950-55; patients with concomitant diabetes were excluded so that for the most part the cases included were those of typical uncomplicated ischaemic heart disease occurring among white males 40 years of age or over. The incidence of ischaemic heart disease per 100 necropsies during the four periods was 12·15, 11·27, 15·13, and 18·44 respectively. By comparing the two earlier with the two later periods it was shown that in the combined period 1935-44 the incidence per 100 necropsies was 11·66, whereas in the period 1945-55 it had risen to 16·98, a statistically significant increase.

Having concluded from the previous study that subjects dying from cancer and from accidents formed a representative sample of the general population, the author then examined the incidence of atherosclerosis and the factors influencing its development by dividing the combined accident and cancer necropsy records into two groups according to whether death occurred in the period 1935-44 or 1945-55, these being further divided into four subgroups according to age at time of death. This revealed that more persons were free of atherosclerosis in each age group in 1935-44 than in 1945-55; moreover the incidence of advanced atherosclerosis was

greater in each age group during the latter period. More advanced atherosclerosis was also found in hypertensive patients, especially those in the older age groups. No conclusions, however, could be reached concerning the association between body weight and coronary atherosclerosis.

Eirlan Williams

368. Epidemiology of Ischemic Heart Disease among White Males. III. Role of Coronary Atherosclerosis and Clot Formation in Patients with Ischemic Heart Disease H. M. Parrish. *Journal of Chronic Diseases* [J. chron. Dis.] 14, 339–354, Sept., 1961. 35 refs.

In this third study the 2,731 necropsy records previously used [see Abstracts 366 and 367] were analysed to test the hypothesis that in patients with ischaemic heart disease atherosclerotic obstruction is less severe than it was 20 years ago and that coronary thrombosis is now more prevalent. The records of non-diabetic patients with ischaemic heart disease were divided as before into the two periods 1935–44 and 1945–55, and these into subgroups according to age at death.

In all age groups significantly more severe obstruction from atherosclerosis was found in the earlier period, but while the results suggested a higher incidence of coronary arterial thrombosis among young patients in the period 1945-55 the difference was not statistically significant. All patients with ischaemic heart disease were shown to have coronary atherosclerosis, but in only 53% were coronary clots found, a finding tending to support the theory that clot formation is dependent on the presence of atherosclerosis. The degree of coronary atherosclerotic blockage among patients with ischaemic heart disease was unrelated to the presence of hypertension, but fewer hypertensive patients of all age groups had coronary artery clots than had non-hypertensive patients. The severity of atherosclerosis was unrelated to body weight at the time of death, but coronary clots were found in 62% of overweight patients with ischaemic heart disease, compared with 48% of those of average weight and 27% of those who were underweight.

The hypothesis that patients with ischaemic heart disease suffer from abnormal blood coagulation was supported by the finding that a higher percentage of these patients than of patients with cancer in all age groups had extracardiac clots, but on the other hand extracardiac clots were no more common in patients with ischaemic heart disease with coronary clots than in those without such clots.

Elrian Williams

369. Fibrinolytic Treatment of Coronary Thrombosis: a Pilot Study

H. A. DEWAR, A. R. HORLER, and A. J. CASSELLS-SMITH. British Medical Journal [Brit. med. J.] 2, 671-675, Sept. 9, 1961. 4 figs., 18 refs.

Thrombolysin (human plasminogen activated by streptokinase) infused into the coronary arteries of dogs has been shown to cause lysis of artificially induced thrombi, and fibrinolytic agents have since been prescribed to human subjects suffering from myocardial infarction and other thrombotic disorders. In the investigation here

reported from the Royal Victoria Infirmary, Newcastle upon Tyne, thrombolysin was given intravenously to a group of patients with cardiac infarction to establish whether the treatment was safe, whether it was potent, and whether it had a beneficial effect on the course of the disease. Of a series of 33 patients admitted to hospital within 12 hours of the onset of pain, 17 (15 men and 2 women of average age 60·2 years) received thrombolysin and the remainder (15 men and one woman of average age 59·4 years) served as controls.

Through a fine-bore polythene cannula or Guest-type cannula inserted into a forearm vein an initial dose of 25,000 units of thrombolysin freshly dissolved in 5% glucose in water was infused rapidly over-a few minutes followed by a further 25,000 units over the next hour and thereafter 50,000 units hourly for 11 hours to a total dose of 600,000 units. The control patients received infusions of glucose solutions only. Electrocardiograms (ECGs) were recorded every 8 hours for the first 2 days and then daily for a further 10 days. All patients were treated with anticoagulants, though these were

withheld for the first 15 hours in order not to interfere

with the estimation of fibrinolytic activity; patients were usually kept in hospital for 3 weeks.

A comparison of the fibrinolytic activity of the blood in 10 of the treated cases with that in 6 of the controls established the potency of the thrombolysin, All patients showed some increase above normal values, as has previously been observed after cardiac infarction. but in 5 of the treated patients a marked increase in fibrinolytic activity was maintained during a substantial part of the infusion. There was little correlation between fibrinolytic activity and the level of plasma fibrinogen, although in 5 of the treated patients the level of fibrinogen fell below 0.2 g. per 100 ml. In 3 treated patients severe hypotension necessitated the use of pressor drugs; otherwise no serious side-effects were observed. Five of the treated patients died as opposed to one of the controls, but the numbers were considered too small for these differences in mortality to be significant. Similarly, any beneficial effect which thrombolysin may have had on the evolution of the infarct was not apparent on clinical examination or by comparing serial changes in the ECG. When consecutive transaminase levels in blood withdrawn every 4 hours for 16 hours and then daily for 12 days were plotted against the time of onset of pain, however, the curves obtained from 10 treated patients were taller and narrower than those obtained from 10 controls. This was attributed to a more rapid liberation of enzyme and gave support to the suggestion that reperfusion of the infarct had occurred as a result of lysis either of the primary thrombus or of thrombi in the Eirian Williams collateral channels.

370. Liver Function in Acute Myocardial Infarction: a Study using Bromsulphthalein Test

A. J. ROSIN. British Medical Journal [Brit. med. J.] 2, 675-677, Sept. 9, 1961. 9 refs.

The abnormalities of liver function which may occur in the acute stage of myocardial infarction were studied in 20 patients admitted to the Royal Alexander Infirmary, Paisley. The "bromsulphalein" (B.S.P.; sulphobromophthalein) test was performed in each case within a few hours of admission, as well as estimations of serum bilirubin level, thymol turbidity, zinc sulphate turbidity, serum alkaline-phosphatase level, and the blood urea level.

Abnormal B.S.P. retention was found in 15 patients and it was more marked in the presence of shock, but on the other hand in 2 patients with mild or minimal shock the result of the test was normal. The other tests of liver function were normal in all except 2 patients in whom the serum bilirubin level was slightly raised (1 to 3 mg. per 100 ml. and 1 mg. per 100 ml. respectively) and in a third with a serum alkaline-phosphatase level of 26·3 units. There was no correlation between abnormal B.S.P. retention and elevation of the blood urea level.

Eirian Williams

371. An Assessment of Erythrocyte Migration Times and Serum Cholesterol Levels as Indices in Myocardial Infarction

D. F. DAVIES and A. CLARK. Clinical Science [Clin. Sci.] 20, 279-287, June, 1961. 6 refs.

The electrophoretic migration time of erythrocytes and the serum cholesterol levels were studied in two groups of patients with myocardial infarction at the War Memorial Hospital, Wrexham, and the West Wales General Hospital, Carmarthen. At each hospital the findings in 25 patients with myocardial infarction were compared with those in a group of 25 controls without evidence of infarction or atheroma, the groups being matched for age.

The findings were similar in both hospitals. There was a significantly prolonged erythrocyte migration time in both groups with myocardial infarction, and while the mean serum cholesterol level was raised in these groups as compared with controls, the difference was of a lower order of significance than that found for erythrocyte migration time. It is suggested that an increase in erythrocyte migration time is more closely related to the aetiology of myocardial infarction than is an increase in the serum cholesterol level. Patients with myocardial infarction and the shorter erythrocyte migration time tended to have a higher serum cholesterol level. Conversely, the greatest increase in the erythrocyte migration time was observed in patients with the lowest serum cholesterol levels. Thus the two indices mutually support each other and when used together efficiently differentiate patients with infarction from controls.

C. Bruce Perry

372. The Behaviour of the Eosinophil Leucocytes in Myocardial Infarction. (Il comportamento degli eosinofili nell'infarto miocardico)

C. BAROCELLI and G. BARBANO. Minerva medica [Minerva med. (Torino)] 52, 3351-3357, Sept. 29, 1961. 6 figs., 17 refs.

The authors have previously observed a marked eosinopenia (less than 50 eosinophils per c.mm.) in patients suffering from myocardial infarction. In this paper they describe further results in 87 patients with infarction admitted to the Ospedale Maria Vittoria, Turin. A series of 71 patients with angina pectoris but without infarction served as a control group.

In the majority of such cases the eosinophil count returns to 50 per c.mm. or more on the 5th day of the illness, but in this series 11 of the 80 surviving patients had a persistent eosinopenia on the 7th day, the count in the other 69 having returned to normal. Of these 69 patients, 4 (6%) died within 2 months, whereas of the 11 with persistent eosinopenia, 5 died, all within 27 days, a mortality of 45%. In the control group without infarction the eosinophil count never, with the exception of one case, fell below 50 per c.mm. The authors suggest that marked eosinopenia following myocardial infarction is an expression of Selye's alarm reaction and that it has a serious prognostic significance when it persists beyond the seventh day.

A. J. Karllsh

373. Treatment of Cardiac Arrest in Acute Myocardial Ischaemia and Infarction

D. G. JULIAN. *Lancet* [Lancet] 2, 840-844, Oct. 14, 1961. 3 figs., 12 refs.

The author describes the treatment of 5 patients admitted to the Edinburgh Royal Infirmary with acute myocardial ischaemia or infarction who collapsed in the ward with ventricular fibrillation or asystole. Cardiac massage through the open chest or by the closed-chest technique was carried out, a defibrillator was used, and, in 3 cases, an endotracheal tube was passed. In 4 of the patients normal rhythm was restored with satisfactory blood-pressure levels. One patient whose chest was opened within 3 to 4 minutes of the initial collapse was alive a year later. Three patients died 2 hours, 2 days, and 11 days after resuscitation respectively. In the remaining case resuscitation was started after 10 minutes, but the heart could not maintain atrial or ventricular rhythm for more than a few seconds.

The author attributes the complications in these patients to delay in starting cardiac massage and to errors in technique. He suggests that lives could be saved if medical, nursing, and auxiliary staff were trained in closed-chest cardiac massage, and that in patients with recent acute myocardial infarction cardiac rhythm should be monitored by an electrocardiogram linked to an alarm system in special intensive therapy units.

I. Ansell

374. Myocardial Infarction in the Younger Age Groups. I. Clinical Review of Cases up to the Age of 55. [In English]

R. MALMCRONA, P. BIÖRNTORP, B. SÖDERHOLM, O. THULESIUS, and F. HEYMAN. *Acta medica Scandinavica* [Acta med. scand.] 170, 301-311, Sept., 1961. 1 fig., 27 refs.

The authors present the first part of a study of all patients who developed myocardial infarction below the age of 55 and who were admitted to the City Hospital, Göteborg, Sweden, in the 9 years 1948 to 1956. During this period there were 404 such cases, but when the diagnoses were carefully scrutinized only 318 (253 in men and 65 in women) fully satisfied the clinical, electro-

cardiographic (ECG), and post-mortem criteria laid down for this study.

No obvious predisposing causes were found in 165 (32%) of the patients. Diabetes was present in 15 (5%). hypertension in 126 (40%), essential familial hypercholesterolaemia in 6, and hypothyroidism in 5. There was no difference in the age incidence of the various groups. However, 7 (50%) of those with diabetes as the sole predisposing cause were women, as opposed to only 20 (12%) of the 165 with no obvious predisposing cause and 29 (24%) of those with hypertension. The over-all mortality for the whole period was 42% (40%) for men and 50% for women). The highest death rate occurred in the first month, and of those patients who died after the first month, 49% were known to have had a further infarction; however, 19% of the survivors had also had repeated infarction. Factors adversely influencing the prognosis were greater age and the presence of diabetes or severe hypertension. Major ECG changes were associated with a higher death rate than wereminor changes confined to ventricular repolarization. Bundle-branch block was present in 5% of the cases and complicated the electrocardiographic diagnosis.

C. Bruce Perry

375. The Post-myocardial Infarction Syndrome C. Samaras, M. Kolettis, and C. Papaconstantinu. Diseases of the Chest [Dis. Chest] 40, 330-337, Sept., 1961. 14 refs.

Manifestations of the post-myocardial infarction syndrome were studied in 15 out of 175 cases of myocardial infarction seen at the Evangelismos Hospital, Athens, between 1954 and 1960. In 8 typical cases the three principal features of the syndrome were present-namely, continued pyrexia, pain of pleuropericardial type. and an increase in the erythrocyte sedimentation rate (E.S.R.). Less constant features were leucocytosis, exudative pleural effusion (which was haemorrhagic in one case), eosinophilia, pericardial effusion, and anaemia. The syndrome usually developed 1 to 8 weeks after infarction, but in one patient who had had anginal attacks previously it apparently developed before the infarction. There was no correlation between the occurrence of the syndrome and the age of the patient or the site of the infarction. Recurrences of the syndrome were frequent; one patient had recurrences up to 4½ years after the attack of myocardial infarction. In 4 patients the syndrome was incomplete, only two of the three main features being present; one of these patients had periarthritis in addition. In the 3 remaining cases in the series the increase in the E.S.R., for which no cause was found, persisted long after the attack of infarction; the authors suggest that this prolonged increase in the E.S.R. in these cases is probably a monosymptomatic form of the syndrome.

In a discussion of some of the literature on the postinfarction syndrome the authors point out that serous membranes other than pleura and pericardium can be affected—for example, the peritoneum and the synovial membranes. The aetiology of the condition is unknown, but autosensitization resulting from myocardial necrosis may play a part, a suggestion which finds support in the beneficial effects of corticosteroids in the treatment of the syndrome (as occurred in one case in the present series). Gerald Sandler

HYPERTENSION

376. The Basilar Artery Hypertensive Syndrome B. M. Montgomery. Archives of Internal Medicine [Arch. Intern. Med.] 108, 559-569, Oct., 1961. Bibliography.

In this paper from the Medical College of Georgia, Augusta, the author describes 3 patients suffering from paroxysmal hypertensive attacks associated with neurological signs of basilar artery insufficiency. In 2 patients the neurological signs—dysphagia, dysarthria, eye deviation, and fleeting paralyses—although closely associated with the hypertensive attacks, developed only as a later phase in the condition. The author discusses the implication that focal ischaemia in strategic areas of the brain can cause hypertension and that paroxysmal hypertension can be considered part of the syndrome of basilar artery insufficiency.

The causes of paroxysmal hypertension are discussed. The conditions in which organic interim findings are not prominent are chromaffinoma, functional neurogenic hypertension, familial autonomic dysfunction, intermittent insufficiency of the basilar-vertebral arterial circulation, and hypoglycaemia. Those in which organic interim findings are prominent are tabes dorsalis, brain tumour, paraplegia, porphyria, lead poisoning, angina pectoris, intermittent claudication, concussion, and subarachnoid haemorrhage.

E. H. Johnson

377. The Use of Chlorothiazide or Hydrochlorothiazide with Reserpine in the Office Treatment of Hypertension D. B. FISHBACK and L. H. CASTOR. *Diseases of the Chest* [Dis. Chest] 40, 203-209; Aug., 1961. 5 figs., 12 refs.

This paper reports the results of the treatment in private practice of 60 patients with fixed essential hypertension by means of tablets containing hydrochlorothiazide, reserpine, and potassium chloride [proportions not stated]. Many of the patients had previously received reserpine with or without chlorothiazide and were changed over to the combined tablet with the addition of extra reserpine where necessary in the early stages. A large number of these patients had been under observation for periods as long as 10 to 30 years, and none for less than one year before starting this therapy. The follow-up period ranged from 2 to 30 months. No system of control by means of placebos was attempted. All patients were instructed to restrict their intake of sodium and to take fruit juices with a high potassium content.

There was a significant fall in blood pressure in all but 4 of the patients on this regimen. [No details are given of dosage schedules.] Some side-effects from the treatment occurred in 20 of the 60 patients, the most common complaint being a feeling of weakness. This appeared to be related to potassium deficiency and the potassium content of the combined tablet was not always adequate

to compensate for the loss of potassium in the urine. Patients already receiving digitalis showed signs of toxicity soon after starting the treatment, but this, together with the anorexia complained of by a few patients, responded to additional dietary potassium in most cases, although 4 patients refused to accept even a lower dose of potassium. It was found that many patients previously unable to tolerate the requisite hypotensive dose of reserpine alone because of its side-effects could accept the lower dosage on this regimen with equally good results and no evidence of toxicity.

In the authors' opinion treatment with a combined fixed-dosage tablet of hydrochlorothiazide, reserpine, and potassium chloride is successful and practical for the prolonged treatment of mild and moderately severe benign essential hypertension.

[This paper would have been of greater value if details of dosage had been included and a fuller explanation given of the high incidence of side-effects. The reasons for the authors' preference for a fixed-dose tablet in the face of its manifest disadvantages remain obscure.]

J. Warwick Buckler

378. Mecamylamine and Chlorothiazide in the Treatment of Hypertension in Out-patients

G. A. BOUSVAROS. British Journal of Diseases of the Chest [Brit. J. Dis. Chest] 55, 208-215, Oct., 1961. 4 figs., 13 refs.

The author of this paper from the Postgraduate Medical School and Hammersmith Hospital, London, describes the results obtained with mecamylamine and chlorothiazide in the treatment of 30 patients with a persistently raised diastolic blood pressure (110 mm. Hg or more) without azotaemia. All except 2 of the patients received both drugs; 2 received mecamylamine alone throughout the trial. In 11 cases mecamylamine in a daily dosage of 10 to 80 mg. (average 36 mg.) lowered the blood pressure from an average of 207/115 mm. Hg to 181/102 mm. Hg. When chlorothiazide in a dosage of 0.5 g. daily was added to the regimen it was possible to reduce the average dosage of mecamylamine by 47% without loss of hypotensive effect. In 19 patients receiving both drugs from the beginning of the trial the average final daily dose of mecamylamine was 5 to 35 mg. and the fall in average blood pressure was from 211/122 mm. Hg to 184/108 mm. Hg. In the majority of the patients there was significant improvement in retinopathy and hypertensive heart disease. Although most of them were not given potassium supplements, only 2 showed electrocardiographic evidence and only one the clinical features (muscular weakness) of hypokalaemia. There was gradual tolerance to mecamylamine. The usual side-effects of ganglionic blockade were partially relieved by parasympathomimetic drugs.

K. G. Lowe

379. Reorientations in Hypertensive Disorders. [Croonian Lectures]

J. McMichael. British Medical Journal [Brit. med. J.] 2, 1239–1244, Nov. 11, 1961, and 1310–1314, Nov. 18, 1961. 5 figs., bibliography.

Haematology

380. Treatment of Classic Hemophilia: the Use of Fibrinogen Rich in Factor VIII for Hemorrhage and for Surgery

C. W. McMillan, L. K. Diamond, and D. M. Surgenor. New England Journal of Medicine [New Engl. J. Med.] 265, 224-230, Aug. 3, 1961, and 277-283, Aug. 10, 1961. 5 figs., 26 refs.

Classic haemophilia is usually due to a quantitative deficiency of AHG (antihaemophilic globulin; Factor VIII), though a few cases may be complicated by excess production of an ill-defined inhibitor of Factor VIII. Treatment usually consists in the intravenous infusion of fresh normal human plasma and it is to some extent limited by the amount of fluid which can be given. It is usually adequate in the management of closed soft-tissue injuries, but it may be difficult to achieve the plasma Factor-VIII activity required for haemostasis in trauma or surgery. Factor VIII has proved difficult to isolate, and this paper from the Children's Hospital Medical Center, Boston, reports on the use of a commercially available fibrinogen fraction rich in Factor VIII.

The fibringen, fraction was derived from Cohn's Fraction I and it was used in the treatment of 15 patients with haemophilia presenting a variety of haemorrhagic and surgical conditions. The fraction produced the expected rise in plasma Factor-VIII activity as measured by the thromboplastin generation test and was effective in securing haemostasis in primary haemorrhagic states. For control of bleeding at operation plasma Factor-VIII activity of 30 to 60% was required initially and meticulous local haemostasis was also essential. The necessary levels of Factor VIII could be attained with the fibrinogen fraction except in those haemophiliacs who apparently had a Factor-VIII inhibitor. All patients undergoing prolonged replacement therapy with this new factor showed marked clumping of erythrocytes associated with hyperfibrinogenaemia; in 2 patients transient haemolytic phenomena were observed.

It is suggested that the fibrinogen fraction rich in Factor VIII is superior to fresh plasma in the replacement therapy of classic haemophilia. The main advantages of the new fraction are the smaller volume required and the achievement of higher Factor-VIII activity in the recipient's plasma.

A. Brown

381. The Thrombocytopenic Effect of Sustained Highdosage Prednisone Therapy in Thrombocytopenic Purpura P. Cohen and F. H. Gardner. New England Journal of Medicine [New Engl. J. Med.] 265, 611-617, Sept. 28, 1961. 10 figs., 26 refs.

The authors report that of 7 patients with thrombocytopenic purpura (in 3 cases secondary to disseminated lupus erythematosus and in 4 idiopathic) who were treated at the Peter Bent Brigham Hospital, Boston, with high doses of prednisone (30 to 100 mg. daily) for 2 or

more weeks, all showed a fall in the platelet count during treatment. The hypothesis that this was due to increased platelet destruction (which required a still higher dose of steroids) is rejected on the grounds that the slow rectilinear decline from the peak platelet level indicated a normal platelet life span with reduced production of platelets in the marrow. In one patient the platelet life span, estimated by labelling with radioactive chromium, was shown to be normal under these conditions. Furthermore, in 4 of the patients a reduction in the dose of prednisone was followed by an increased platelet count. It is considered that sustained high doses of prednisone suppress production of platelets in bone marrow.

P. C. Reynell

382. Hypogammaglobulinaemia in Chronic Lymphatic

G. H. FAIRLEY and R. B. SCOTT. British Medical Journal [Brit. med. J.] 2, 920-924, Oct. 7, 1961. 6 figs., 48 refs.

The impaired formation of circulating antibodies in patients with chronic lymphatic leukaemia is often accompanied by an abnormal level of gamma globulin in the serum. In the present study the serum gammaglobulin levels were estimated in 110 patients with chronic lymphatic leukaemia and in 55 healthy controls at St. Bartholomew's Hospital, London. Serum total protein values were determined by the biuret method and the various protein fractions by passing the electrophoretic strips through an electrodensitometer. Good correlation was obtained between two immunological techniques, the agar diffusion method of Gell (J. clin. Path., 1957, 10, 67; Abstr. Wld Med., 1957, 22, 83) and the gammaglobulin neutralization method described by Mollison; these techniques were particularly valuable when the serum gamma-globulin level was low.

Four basic gamma-globulin patterns were found. (1) In 29% of the patients the gamma-globulin level was within the normal range. (2) The level was reduced in 67%, and this was shown to be related to the duration of the disease (correlation coefficient r=-0.239, P<0.05); all patients who had had the disease for over 5 years had hypogammaglobulinaemia, but treatment was not responsible, since there was no significant difference between treated and untreated patients or between those given different forms of treatment. (3) In only 3% was the gamma-globulin level raised; and (4) in 1% (one patient) there was macroglobulinaemia (sedimentation constant S_{20w} 19.5). All patients who had suffered from more than 3 infections in a year (as well as 2 patients in whom the first infection was fatal) had hypogammaglobulinaemia. Intramuscular injections of gamma globulin may be given in a loading dose of 0.16 g. per kg. body weight, followed by a maintenance dose-of 0.025 g. per kg. weekly. It is stated that infections in acute leukaemia are not related to hypogammaglobulinaemia. R. B. Thompson

Respiratory System

383. The Neurologic Basis of Cheyne-Stokes Respiration

H. W. Brown and F. Plum. American Journal of Medicine [Amer. J. Med.] 30, 849-860, June [received Sept.], 1961. 7 figs., 39 refs.

From the University of Washington School of Medicine, Seattle, are reported studies on 28 elderly patients with Cheyne-Stokes respiration (C.S.R.) who all had neurological abnormalities and were seriously ill, and for comparison, similar observations on 4 healthy young adults, 3 neurologically intact patients in congestive heart failure, and 7 patients with unilateral or bilateral cerebrovascular disease. All subjects underwent careful clinical and electrocardiographic examination and chest radiography. In all cases, also, measurements were made of venous pressure, circulation time by means of an ear lobe oximeter, arterial blood oxygen saturation and carbon dioxide content, lung gas volumes (by collection or estimation or with a pneumotachometer), and ventilatory response to CO₂ (using a Tissot spirometer). Minute ventilation was also measured and the respiratory threshold for CO₂ was taken as the arterial pCO₂ just sufficient to stimulate respiration in the fully oxygenated subject. Isoventilation curves were constructed for 5 patients to show the relative amount of stimulation to respiration contributed by alveolar CO2 and O2 tensions respectively.

Every patient with C.S.R. had signs of bilateral supramedullary motor dysfunction and all were suffering from hyperventilation and respiratory alkalosis. Peak ventilation coincided with maximum alveolar pCO₂, while apnoea coincided with an alveolar pCO₂ level well below the ventilatory threshold. All these patients also showed about three times the normal sensitivity to CO₂, but ventilation was also increased by reduced O₂ tension. Thus, even when alveolar pCO₂ fell below threshold level hypoxia continued to drive ventilation. The authors conclude that although extracerebral abnormalities may augment ventilatory periodicity, they are not the primary cause of Cheyne-Stokes respiration.

D. Goldman

384. Cerebral Circulation and Function in Cheyne-Stokes Respiration

H. R. KARP, H. O. SIEKER, and A. HEYMAN. American Journal of Medicine [Amer. J. Med.] 30, 861-870, June [received Sept.], 1961. 5 figs., 26 refs.

Of 17 men aged 55 to 70 years with Cheyne-Stokes respiration (C.S.R.) who were studied at the Veterans Administration Hospital, Durham, North Carolina, 15 had vascular disease of the brain or heart, or both, while in the other 2 the symptoms were attributed to gross obesity. Most of these patients were seriously ill and many were semicomatose. In order to determine the changes in cerebral circulation during the phases of

C.S.R., multiple simultaneous arterial and venous blood samples were taken from needles fixed in the brachial artery and jugular bulb.

During the hyperphoeic phase arterial oxygen saturation was lowest, carbon dioxide tension highest, and cerebral arterio-venous O₂ difference decreased. Converse changes were recorded in apnoea. Cerebrospinal fluid pressure was measured in some patients and showed a rise during hyperphoea; during this phase, also, circulation time across the brain, estimated with azovan blue, was shortened, and abnormalities in the electroencephalogram recorded in representative cases often disappeared during hyperphoea, with concurrent improvement in the patient's mental function and consciousness. These latter changes probably result from the phasic alterations in cerebral circulation.

The authors suggest that the circulatory changes and Cheyne-Stokes respiration may both result from an overriding abnormal phasic activity in the central nervous system.

D. Goldman

LUNGS AND BRONCHI

385. Trypsin Therapy in Pulmonary Disease, 1955–1960

H. SHUBIN, J. S. SHERSON, and D. WEISSMAN. *Diseases of the Chest [Dis. Chest]* 40, 148–153, Aug., 1961. 15 refs.

In this study 187 patients, aged 18 to 39 years, suffering from a variety of chest diseases were treated with four different preparations of trypsin. Of the 170 patients who completed the course of treatment, 59 were suffering from chronic bronchitis or bronchial asthma, 48 from pulmonary tuberculosis, 37 from bronchiectasis, 13 from pulmonary emphysema, 14 from unresolved pneumonia. and 9 from abscess of the lung. Full clinical histories and detailed physical examination, together with appropriate special investigations, were carried out monthly before and after treatment. The patients were divided into four groups and treated as follows: (1) 53 patients with pulmonary tuberculosis receiving concomitant antituberculous drugs were given 5 mg. of crystalline trypsin in sesame oil intramuscularly daily for 12 days (15 of these patients refused further injections after the first few days); (2) 30 patients with asthma, bronchiectasis, or atelectasis were given one tablet containing 5 mg. of crystalline trypsin to be taken by mouth twice daily for 14 days; (3) 50 patients with various chronic chest diseases were given 5 mg. of crystalline trypsin in an aqueous gelatin medium intramuscularly daily for 7 to 14 days; and (4) 54 patients with similar diagnoses to those in Group 3 were given enteric-coated tablets containing the equivalent of 20 mg. of crystalline trypsin, 2 tablets being taken four times a day.

It was found that patients in Group 1 derived some symptomatic improvement from the intramuscular injections of trypsin in the sesame oil—when these could be tolerated—and although there was no apparent effect on the tuberculous process other than that expected from the concomitant chemotherapy, the sputum became thinner and expectoration was increased. Of the 30 patients in Group 2 receiving trypsin orally, 17 complained of irritation of the mouth and 5 developed ulceration; the sputum did become somewhat less tenacious, but the improvement was of doubtful significance. The 50 patients in Group 2 tolerated the pain at the injection site better than those in Group 1 and 31 showed moderate or marked improvement in conditions such as unresolved pneumonia with atelectasis, lung abscess, chronic bronchitis, and pulmonary emphysema. Objective evidence of improvement by clinical or radiological criteria was obtained in 13 of these patients, there being liquefaction of bronchial secretions in most patients; no improvement was noted in 4 cases. The results of treatment with the enteric-coated tablets of trypsin (Group 4) were not available at the time of writing, but preliminary impressions were that in 44 of the 54 patients trypsin in this form was as effective as parenteral treatment.

The authors conclude that aqueous trypsin given by intramuscular injection or in the form of enteric-coated tablets is therapeutically effective in certain pulmonary diseases and that it promotes a more rapid clinical improvement in chest disease due to infections in that it seems to enhance the effectiveness of antituberculous drugs and antibiotics.

J. Warwick Buckler

386. A Retrospective Clinical Study of Pulmonary Disease Due to "Anonymous Mycobacteria" in Wales S. R. KAMAT, C. E. ROSSITER, and J. C. GILSON. *Thorax* [*Thorax*] 16, 297–308, Sept., 1961. 3 figs., 35 refs.

A comparative study is reported of 57 patients with anonymous mycobacterial infection and 57 "similarly timed" patients suffering from tuberculosis. These cases were collected through the Tuberculosis Reference Laboratory, Cardiff, between 1952 and 1960. There was a higher percentage of coal-miners with pneumoconiosis in the anonymous group than in the tuberculous group. In about three-quarters of the anonymous group the infection appeared to cause symptoms. Only 2 out of 34 chromogen (Types I and II) strains were asymptomatic compared with 9 out of 23 non-chromogen (Type III) strains. Haemoptysis was twice as common in the anonymous group. Most of the anonymous strains were resistant to 2 or more of the major antituberculous drugs. which still seemed to have some therapeutic effect. The sputum conversion rate was lower in the anonymous than in the tuberculosis group, but the time taken for conversion was the same.

There was a higher incidence of cavitation in the anonymous group especially if pneumoconiosis was present. One-fifth of the anonymous group showed progression of the lesions, compared with only one-tenth of the controls. Reduction in the area of shadowing was associated with sputum conversion; of the patients showing no change or increased shadowing, three-quarters still

had positive sputum. The histology of the resected specimens from 7 anonymous infections closely resembled that of tuberculosis. Radiological evidence of tuberculosis was present in fewer of the contacts of the anonymous group than of the tuberculosis group, but the Mantoux conversion rates were the same for both. In 11 out of 18 patients from whom a single culture of anonymous bacilli was obtained the strains were Type III. - A number of patients had "complicated pneumoconiosis" and in 7 cavitation was present, but few of these men were clinically ill. One patient is described with erythema nodosum, bilateral hilar adenopathy, and sarcoid-like radiological changes associated with Type-III anonymous mycobacteria in the sputum; he responded to antituberculous drugs. I. Ansell

387. Moderate and Severe Pneumococcal Pneumonia: Treatment with Propionyl Erythromych

J. B. HILL, J. LINDNER JR., J. McB. GARVEY JR., J. MILLHON, and M. HAMBURGER. Archives of Internal Medicine [Arch. intern. Med.] 108, 578-582, Oct., 1961. 11 refs.

At the Cincinnati General Hospital, Ohio, 64 patients with moderate or severe pneumococcal pneumonia were treated with propionyl erythromycin. In 29 of the patients other diseases were present and "an undetermined but probably significant percentage" were chronic alcoholics. Of the 64 patients, 57 (89%) responded rapidly to the drug, the average duration of fever being 1.9 days and treatment lasting 3 to 12 days. Complicating diseases were present in 12 of this group and 20 were considered to be seriously ill. A satisfactory but submaximal response was obtained in 5 patients treated for about 14 days; all 5 patients were severely ill and had concomitant diseases. The response to propionyl erythromycin was unsatisfactory in only 2 cases and tetracycline was substituted.

Propionyl erythromycin was given by mouth in a dosage of 250 mg. every 6 hours. In some young patients who were not severely ill the drug was given in a dosage of 250 mg. every 12 hours, with good results. No sensitivity reactions and no gastro-intestinal disturbances were observed. Propionyl erythromycin would seem to be an adequate substitute when there is any reaction to penicillin.

E. H. Johnson

388. A New Mucolytic Agent by Aerosol for Inhalation in Chronic Bronchitis

K. N. V. PALMER. Lancet [Lancet] 2, 802-804, Oct. 7, 1961. 1 fig., 18 refs.

This paper from the University of Aberdeen reports the use of "ascoxal", a tablet containing 100 mg. of ascorbic acid, 70 mg. of sodium percarbonate, and 0·2 mg. of copper sulphate, as a mucolytic agent in chronic bronchitis. The subjects of the trial were 15 patients who had been in hospital for a few days or weeks. They were expectorating mucoid sputum, were not receiving drugs, and were regarded as being in a stable phase. The patients were studied in the afternoon because the author considers that the viscosity of the sputum is most constant at this time.

Approximately 3 ml. of sputum was collected and its viscosity measured in a cone-and-plate viscometer designed for this purpose, the result being expressed in degrees of rotation of the cone, the deflection increasing with viscosity. One tablet of ascoxal was then dissolved in 2 ml. of warm water and nebulized by oxygen in a Collinson apparatus, the particle size being 0.5 to 3.0 μ . The solution was inhaled for 15 minutes. The sputum was collected one hour after the inhalation and its viscosity again measured. The whole procedure was repeated daily for 3 to 5 days. The mean viscosity of the sputum before treatment ranged from 150° to 600° and after treatment from 20° to 440°, the mean reduction in viscosity being 198.8° or 53%.

Experiments were carried out with ascoxal in vitro to assess the time and concentration required to produce maximum mucolysis in sputum. It was found that ascoxal alone produced rapid mucolysis in 10 minutes, but the effect was much less if the drug was diluted.

There were no side-effects when 1 or 2 tablets were used in 2 to 4 ml. of water thrice daily for up to a month. Ascoxal is very much cheaper than trypsin, each inhalation costing 3d. [3½c.] compared with 10s. 6d. [\$1.48] for crystalline trypsin. Hand inhalers do not produce small enough droplets to penetrate the bronchioles and are therefore not recommended. The drug must be given by an apparatus such as the Collinson which produces a fine "dry" mist.

[Most mucolytic agents are useless. This one appears to be more promising.]

I. M. Librach

389. Lang Abscess—a Review of Forty-one Cases
I. F. Rumbauch and J. A. Prior. Annals of Internal
Medicine [Ann. intern. Med.] 55, 223-234, Aug., 1961.
4 figs., 35 refs.

Some aspects in the diagnosis and treatment of lung abscess are discussed with reference to the findings in 41 patients admitted to the Ohio State University Hospital, Columbus, over a period of 5 years. It is first emphasized that in these cases there is often pre-existing pulmonary disease; of the 41 patients, 10 had bronchiectasis, 3 had asthma, one emphysema, and one bronchogenic cysts. Bacteriological examination of the sputum showed evidence of a wide variety of organisms; in 21 out of 23 cases from which serial cultures were obtained a change of flora took place with the emergence of Gram-negative organisms. Bronchography, which is considered to be an important investigation, revealed evidence of bronchiectasis in 10 out of 25 cases. Bronchoscopy was carried out in 15 cases.

Antibiotics were the mainstay of medical treatment, but the authors emphasize that in order to determine the most suitable drug sputum cultures should be examined weekly and individual tolerance to any one antibiotic should be carefully observed. Postural drainage was carried out in some cases and most of the patients received aerosol therapy. In 10 of the 18 patients treated medically there was complete resolution. Analysis of this group showed that all 10 patients had had their symptoms for less than 4 weeks or were known to be free from associated pulmonary disease. Surgical treat-

ment was given to 17 patients because of poor response to medical management (11 cases) or because carcinoma appeared likely. Resection was carried out on 8 patients with satisfactory results and external drainage on 3 with poor results. Of the 41 patients in the series, 31 in whom the primary diagnosis was lung abscess were adequately followed up; of these, 22 (71%) were cured and had no residual disability and 2 died, a mortality of 6.4%.

K. C. Robinson

390. Bacterial Infection and Some Effects of Chemoprophylaxis in Chronic Pulmonary Emphysema. I. Chemoprophylaxis with Intermittent Tetracycline

A. L. DAVIS, E. J. GROBOW, R. TOMPSETT, and J. H. McCLEMENT. American Journal of Medicine [Amer. J. Med.] 31, 365–381, Sept., 1961. 1 fig., bibliography.

At Bellevue Hospital, New York, the authors have observed the effects of chemoprophylaxis with tetracycline in 29 patients aged 45 to 76 years with emphysema and chronic bronchitis. During the period September, 1956, to February, 1958, 16 of these patients selected at random received tetracycline in a dosage of 0.5 g. four times a day for 2 days in each week, the remaining 13 patients being given a similar number of placebo capsules and serving as a control group. Before the start of treatment 3 weekly specimens of sputum were examined and pulmonary function tests performed in each case, while during treatment a specimen of sputum was examined and cultured weekly and a clinical examination carried out monthly by a physician who was unaware of the group to which the patient belonged.

After 6 months' treatment questioning revealed little difference in the subjective state of the patients in the two groups. At the end of 12 months, however, a similar inquiry revealed that 69% of the tetracyclinetreated patients, but only 46% of the placebo group, felt better. Objectively, during the study there were 29 episodes of acute respiratory infection in the treated group and 35 similar infections in the placebo group. In the tetracycline-treated patients Haemophilus influenzae was isolated from the sputum less than half as frequently as in the placebo group. In the former group also pneumococci were seldom found in the sputum, whereas in the placebo group they were isolated from 23:1% of all cultures. Staphylococci appeared in the sputum in both groups, but did not present a serious problem. The correlation between the occurrence of acute respiratory infections and the presence of H. influenzae was low, but somewhat higher with the presence of pneumococci. Pulmonary function tests did not show any improvement as between the tetracycline and placebo groups when compared with each other after treatment or with the respective pre-treatment findings. The authors conclude that intermittent tetracycline prophylaxis as used in this study is of questionable value. Charles Rolland

391. Chronic Pulmonary Emphysema: Anatomy and Pathogenesis

A. G. Heppleston and J. G. Leopold. *American Journal of Medicine [Amer. J. Med.*] 31, 279-291, Aug., 1961. 7 figs., 45 refs.

Endocrinology

392. Chlorothiazide Derivatives for Diabetes Insipidus? C. S. ALEXANDER and G. B. GORDON. Archives of Internal Medicine [Arch. intern. Med.] 108, 218-225, Aug., 1961. 1 fig., 14 refs.

The effect of chlorothiazide and its analogues on urinary excretion in diabetes insipidus is discussed in this paper from the Veterans Administration Hospital and the University of Minnesota, Minneapolis. When chlorothiazide was given intravenously either as a single dose of 500 mg, or as an infusion at a rate of approximately 1 mg, per minute to one patient with acquired and one with nephrogenic diabetes insipidus there was a slight increase in the free water clearance; inulin clearance ratio. In another patient with acquired diabetes insipidus no significant change was noted when an infusion of chlorothiazide was given. When hydrochlorothiazide was given by mouth in a dose of 50 mg, twice daily to the same 3 patients there was a decrease in the volume of urine to one-third to one-half of the control values, with an increase in osmolarity. The reason for this difference in action was not elucidated.

The authors suggest that "these drugs may be tried in selected cases of acquired diabetes insipidus with proper supervision to prevent potassium depletion. They are more specifically indicated in vasopressin-resistant diabetes insipidus in which they are the only drugs known to reduce urine output".

G. S. Crockett

393. A New Test for the Investigation of the Hypophysis: the Metopyrone (SU 4885) Test (with Reference to 18 Personal Observations). (Un nouveau test d'exploration hypophysaire: le test au métopyrone ou SU 4885. (A propos de 18 observations personnelles)) L. DE GENNES, H. BRICAIRE, L. MOREAU, and B. MATHIEU DE FOSSEY. Bulletins et mémoires de la Société médicale des hôpitaux de Paris [Bull. Soc. méd. Hôp. Paris] 77, 511-521, April 28 [received July], 1961. 4 figs., 15 refs.

Metopyrone (SU 4885) inhibits 11-β hydroxylation of steroids so that cortisol production in the adrenal cortex is prevented and corticotrophin production by the hypophysis is increased. The immediate precursor of cortisol. 11-deoxycortisol, does not inhibit corticotrophin secretion so that the increase in the urinary output of the metabolite of 11-deoxycortisol (the tetrahydro compound) is progressive and measurable as Porter-Silber chromogen. The functional capacity of the adenohypophysis can be tested by the administration of metopyrone followed by that of corticotrophin. A negative response to metopyrone may be due to adrenocortical deficiency in which case the response to corticotrophin will also be negative. The test is carried out by measuring the daily urinary excretion of Porter-Silber chromogens and of 17-oxosteroids for 3 days, metopyrone being given orally (0.5 g. every 3 hours or 1 g. every 6 hours) during the second day. If there is no increase, or only a small

one, in excretion of the chromogen then the test is repeated with intravenous corticotrophin (25 mg.) in place of the metopyrone.

In 4 normal subjects chromogen output was doubled on the day of metopyrone administration and trebled or. quadrupled on the following day. The response to corticotrophin was much less. The excretion of 17oxosteroids was hardly altered by metopyrone, though consistently increased by corticotrophin. The chromogen output was increased only slightly or not at all in 7 cases of suspected adenohypophysial deficiency, in all but one of which the response to corticotrophin was normal. It is suggested that the exception (a longstanding case) was attributable to adrenal atrophy secondary to the hypophysial deficiency. The response to metopyrone was normal in 2, subnormal in 2, and absent in 2 cases of haemosiderosis, all of which responded to corticotrophin. There was also a negative response to metopyrone in a case of Cushing's syndrome. In a case of congenital adrenal hyperplasia, pregnanetriol excretion was increased by metopyrone, which did not affect the excretion of Porter-Silber chromogen or of 17-exesteroids

It is concluded that the metopyrone test is an accurate and sensitive method of investigation of hypophysial function, provided that the adrenal cortex is capable of responding to the corticotrophin released.

Peter C. Williams

THYROID GLAND

394. Thyroid Antibodies during Pregnancy, and in the Newborn

R. H. PARKER and W. H. BEIERWALTES. Journal of Clinical Endocrinology and Metabolism [J. clin. Endocr.] 21, 792-798, July, 1961. 1 fig., 5 refs.

It has been suggested that maternal thyroid autoantibodies can be transferred across the placenta and that such antibodies may then produce foetal hypothyroidism. At the University of Michigan Medical Center, Ann Arbor, this hypothesis was tested in 22 women in whom thyroid autoantibodies were found during pregnancy. Six of these women had Hashimoto's disease and were all receiving thyroid extract. Most of the remainder were found by screening a large number of normal women presenting at an antenatal clinic. The incidence of detectable thyroid antibodies in the normal pregnant women was the same (4%) as that in a group of non-pregnant women of similar ages attending other out-patient departments.

The titres fell during pregnancy in all but 2 of 10 mothers in whom repeated quantitative studies were made. These 2 patients were tested only during the latter half of pregnancy; in those followed throughout pregnancy the greatest fall in titre was shown usually to

occur during the early months, while in the great majority the titres rose again within a few months of parturition. No antibodies were found in the cord blood of infants born to mothers whose antibody titres had fallen to zero. Antibodies were, however, demonstrated in the cord blood of 8 out of 9 infants whose mothers' blood showed antibodies at the time of delivery. These antibodies disappeared from the blood of all the infants within 3 months. No clinical or laboratory evidence of hypothyroidism was found in them at birth or subsequently. The transplacental carriage of thyroid autoantibodies is therefore confirmed, but no evidence for the actiological importance of such antibodies in the causation of cretinism was obtained.

H.-J. B. Galbraith

395. The Thyroid Gland after Age 50 R. P. Stoffer, C. A. Hellwig, J. W. Welch, and E. N. McCusker. Geriatrics [Geriatrics] 16, 435-443, Sept., 1961. 11 figs., 16 refs.

At the Hertzler Clinic and Research Foundation, Halstead, Kansas, a comparative histological study of the thyroid glands from 141 subjects aged 50 to 95 years and from 72 subjects aged 13 to 39 years showed that the average diameter of thyroid follicles was highest in the third decade of life, decreasing rapidly between 30 and 50 years and more slowly at older ages. There was some loss of average height of follicle cells with age together with some increase in fibrous stroma, and the colloid tended more often to stain basophilically. The authors conclude that enough functional units remain to meet the demands of the ageing organism.

The serum protein-bound iodine levels in 178 elderly euthyroid patients were at least as high as those in younger subjects, but in the older age group the rate of radio-active iodine accumulation was lower. This apparent discrepancy is explained by assuming a lowered rate of tissue utilization of hormone in older people. It is argued that thyroid involution after the age of 50 is a reaction to decreased requirements and not a primary cause of ageing.

J. N. Agate

396. Myxedema, Shock and Coma: Seven Survival Cases

B. CATZ and S. RUSSELL. Archives of Internal Medicine [Arch. intern. Med.] 108, 407-417, Sept., 1961. 7 figs., 33 refs.

The authors describe 11 cases of myxoedema with shock and coma and one case of myxoedema with shock but without coma. The ages of the patients (5 male and 7 female) ranged from 47 to 85 years, 9 being over 60 years. With one exception, that of a 77-year-old female who went into shock during induction of anaesthesia for surgical treatment of a fractured femur, the onset of shock with a sudden fall in blood pressure was preceded by an infection, in most cases pneumonia. In several patients there were overt signs of myxoedema, but hypothermia, which has been observed by other workers, was not a feature. The serum chloride and serum sodium levels, which were determined in 8 of the patients, were reduced. Of the 12 patients 5 died.

The authors state that administration of triiodothyronine in a dosage of 25 to 100 µg. daily, associated with corticosteroids, vasopressor drugs (phenylephrine in the present series), antibiotics, and electrolytes is essential in the treatment of this condition. After recovery triiodothyronine was gradually replaced by thyroid extract in doses sufficient to control the myxoedema. Of the 5 patients who died 2 were in congestive cardiac failure on admission and 2 required a tracheostomy. The authors consider that their results are encouraging, the survival rate comparing "very favourably" with rates reported in the literature.

H. F. Reichenfeld

397. Golter and Myxedema from Iodine
I. CAPLIN, G. F. PARKER, J. H. HALL, and H. KHAJEZADEH. Journal of Allergy [J. Allergy] 32, 402-405, Sept.Oct., 1961. 12 refs.

In recent years a number of cases of goitre with or without myxoedema occurring during iodine therapy have been reported. The authors of this paper from the Methodist Hospital Allergy Clinic, Indianapolis, Indiana, describe 3 asthmatic patients who had been receiving potassium iodide for periods varying from 7 months to 2 years. In all 3 patients the thyroid gland became diffusely enlarged and in one of them, an adult, there were also typical signs of myxoedema (grossly reduced basal metabolic rate, raised serum cholesterol level, and a slow pulse rate), which were not seen in the other 2 patients who were both aged 13 years. Withdrawal of the iodine preparation or administration of thyroid extract resulted in the disappearance of the myxoedema within days or weeks and of the goitre over a period of several months. H. Herxheimer

398. Myxedema following Radioactive Iodine Therapy of Hyperthyroidism

R. L. SEGAL, S. SILVER, S. B. YOHALEM, and S. FEITEL-BERG. American Journal of Medicine [Amer. J. Med.] 431, 354-364, Sept., 1961. 37 refs.

This paper reviews the incidence of myxoedema in a series of 1,603 hyperthyroid patients who were treated during the past 12 years with radioactive iodine (131 I) at Mount Sinai Hòspital, New York, in a dosage estimated to provide approximately 100 μ c. of 131 I retained per gramme of thyroid weight. This dosage was reduced by 20% for patients under 40 years of age and increased by 20% for those over 60. The diagnosis of myxoedema was made chiefly on clinical grounds. The disorder was considered to be permanent if replacement therapy was required indefinitely, and to be transient if normal thyroid function succeeded a period of replacement therapy.

Of the 1,603 patients 1,252 were considered to be euthyroid at final evaluation, 112 (8%) had permanent myxoedema, and 28 had died while euthyroid; of the remaining 211 cases 208 were lost to follow-up for various reasons and 3 were still under treatment. The sex of the patient, the presence of eye signs, and the type of goitre (nodular or diffuse) were not found to influence the incidence of myxoedema. There was a higher incidence of myxoedema in young patients, in patients with a single

thyroid nodule, in those with a small thyroid gland, and in those who required only one dose of 131I. Also, the incidence was higher in patients previously treated with x-irradiation or by surgery than in those previously treated with antithyroid drugs. It was also noted that the incidence of permanent myxoedema tended to fall the later the year of treatment, being 16.3% among the patients treated during 1947 to 1949 and only 3.8% for those treated in 1954. The authors attribute this in part to an improvement in the methods of estimating the correct therapeutic dose, as well as of course to the shorter period of follow-up. In most cases the myxoedema began within 8 months of treatment. Transient myxoedema occurred in 103 patients (7%) and in 16 of these cases lasted for more than 6 months; however, all were euthyroid at the final evaluation.

Charles Rolland

399. System of Radioiodine Therapy for Thyrotoxicosis and Nontoxic Goiter Involving Measurement of Thyroidal Radiosensitivity

J. MYHILL, T. H. ODDIE, F. F. RUNDLE, I. B. HALES, and I. D. THOMAS. *Journal of Clinical Endocrinology and Metabolism* [J. clin. Endocr.] 21, 817-825, July, 1961. 13 refs.

Owing to the difficulty in estimating the exact dose of ¹³¹I required in the treatment of thyrotoxicosis the methods in general use at present involve either a relatively high incidence of subsequent myxoedema or, with the multiple small dose technique, an often dangerous delay before euthyroidism is achieved. An attempt was therefore made at the Royal North Shore Hospital, Sydney, to attain greater accuracy of dosage by considering in each patient the radiosensitivity of the thyroid tissue.

Such radiosensitivity was first assessed in a series of patients with goitre by comparing the thyroidal clearance of 131I before and after treatment and then estimating the dose of the therapeutic ¹³¹I actually retained in the gland, this estimate being based on the relative clearances of 131I by the thyroid and kidney respectively. Construction of the mathematical equations necessary to provide a numerical factor for radiosensitivity involved certain assumptions. However, the sensitivity factors, based on these assumptions, of all patients with goitres of a similar size were found to be of statistically normal distribution. The only characteristic which appeared to influence the sensitivity factor was the size of the goitre. No statistical difference in the sensitivity factors was seen between hyperthyroid and euthyroid goitrous subjects, between women and men, or between those with diffuse and those with nodular glands.

From information derived from the study of 181 patients with proven hyperthyroidism, probable hyperthyroidism, or simple goitre, who were divided into four groups according to the size of the thyroid gland, the maximum radiosensitivity in each group was determined. This knowledge of the maximum radiosensitivity likely in a gland of a particular size was then applied to the calculation of the dosage of ¹³¹I in the treatment of hyperthyroidism. By this means the authors have been able to achieve cure with one dose in 50% of patients and with two doses in another 38.5%; only 2% have so

far become myxoedematous. It is thought that an improvement in these figures can be obtained by more accurate application of the method and that a still greater improvement would follow the development of a satisfactory scientific technique for the measurement of thyroid gland mass.

H.-J. B. Galbraith

400. Serum Precipitin Reaction in Hashimoto's Thyrol-

J. M. Moore. Journal of Clinical Pathology [J. clin. Path.] 14, 533-535, Sept., 1961. 3 figs., 3 refs.

In addition to the specific precipitins found in the serum of most patients with Hashimoto's disease, the serum of certain of these patients contains a non-precipitating antithyroglobulin factor which causes clearing of the normal slight opacity of an agar medium. Serum containing this second factor also has the property of inducing precipitating powers in sera previously found to give a negative precipitin reaction. The study here reported from Stobhill General Hospital, Glasgow, was carried out on 2 patients whose sera contained the non-precipitating antithyroglobulin factor and showed the associated enhancing property.

One patient presented as a fairly typical case of Hashimoto's disease. However, one year after the "clearing", non-precipitating, serum component had been detected the goitre rapidly enlarged and became painful. Because of suspected malignancy partial thyroidectomy was performed and histological changes characteristic of "struma reticulosa" were found. At different phases of the illness the precipitating and clearing factors were found at times separately and at times together in this patient's serum. The second patient suffered from splenomegaly and hypersplenism of unknown cause.

The serum of the first patient was the more effective in enhancing the precipitation reaction of sera from patients with Hashimoto's disease which had previously been precipitin-negative. The response of the sera from over 50 cases of Hashimoto's disease (many already under treatment for some time) to the enhancing effect of the special sera was investigated. In those sera which had already shown a positive precipitin reaction no further increase in the degree of precipitation was noted except in a few with very weak initial reactions. Over half of those sera which were previously precipitinnegative showed a positive reaction when tested in the presence of the special, enhancing, serum.

H.-J. B. Galbraith

401. Iodine Metabolism in Hashimoto's Thyroiditis W. W. Buchanan, D. A. Koutras, W. D. Alexander, J. Crooks, M. H. Richmond, E. M. Macdonald, and E. J. Wayne. Journal of Clinical Endocrinology and Metabolism [J. clin. Endocr.] 21, 806-816, July, 1961. 4 figs., 32 refs.

At the Western Infirmary, Glasgow, 40 patients with untreated Hashimoto's disease have been studied by an extensive range of radioactive iodine (131I) and biochemical tests. Each patient had a goitre, as well as a positive precipitin reaction for autoantibodies and/or characteristic histological changes in the gland.

The results of the tests were by no means consistent from case to case, but from a study of the patients as a group a fairly common pattern of iodine metabolism was apparent. The serum protein-bound iodine levels were in the low normal or hypothyroid ranges even in those clinically apparently euthyroid. However, the uptake of stable iodine by the thyroid gland was normal. suggesting that in Hashimoto's disease, while the ability of the gland to trap and retain iodide is maintained, its capacity to form hormone is impaired. The impairment of hormone synthesis would appear to result from more than one metabolic defect, since impairment of organic binding of iodine was shown in several cases by means of a potassium perchlorate discharge test, and also because abnormal, butanol-insoluble, iodinated proteins were often found in high concentrations in the serum. Both abnormalities were sometimes present in the same patient.

The thyroidal uptake of 131I varied widely, but tended to be normal or increased; the serum levels of proteinbound 131I at 48 hours were also often high. From this and certain additional evidence the authors deduce that there is an increased rate of turnover of iodine within the gland, accompanied by a reduction in the size of the intrathyroidal pool of exchangeable iodine. That the rate of iodine turnover reaches the maximum of which the gland affected by Hashimoto's disease is capable is suggested by a lack of response to exogenous thyrotrophin, which produced no further increase in the turnover rate. The abnormal (butanol-insoluble) proteinbound iodine substances are found in similar proportions in both chemical and radioisotopic protein-bound iodine fractions in Hashimoto's disease and so cannot be responsible for the discrepancy described between the levels of the latter. It is concluded that the disturbances of thyroid metabolism in Hashimoto's disease thus resemble those seen in congenital dyshormonogenesis.

H.-J. B. Galbraith

402. Effect of Hypophysectomy on Thyroid Function. [In English]

B. SKANSE. Acta endocrinologica [Acta endocr. (Kbh.)] 38, 166–180, Oct., 1961. 5 figs., 25 refs.

Working at Malmö General Hospital (University of Lund), Sweden, the author has studied thyroid function before and after hypophysectomy in 10 patients with metastasizing carcinoma of the breast.

After hypophysectomy the thyroid uptake of ¹³¹I, the serum protein-bound iodine level, and the basal metabolic rate (B.M.R.) all fell to the values seen in myxocdema, but in only 3 did the serum cholesterol level rise to a similar degree. Compared with the values found before operation the administration of thyrotrophic hormone after hypophysectomy produced a smaller increase in the uptake of ¹³¹I in 2 out of the 10 and a smaller increase in the serum protein-bound iodine level in 4, 2 of whom had a decreased ¹³¹I uptake. On the other hand the effect of thyrotrophic hormone on the B.M.R. was greater in 3 out of 10 cases and that on the serum cholesterol level greater in 6 out of 9 cases after than before the operation. In the remainder the results before and after operation were comparable.

During thyroid replacement therapy the responsiveness to thyrotrophic hormone decreased further in 3, and probably 4, out of 5 cases.

Although in all these patients it was considered on clinical and laboratory grounds that the hypophysectomy had been complete, at post-mortem examination it was found to be complete in only 5. The clinical effect on the basic disease did not seem to depend on the histological completeness of the hypophysectomy, and neither did the resulting depression of thyroid function.

After hypophysectomy, thyroid ¹³¹I uptake and the serum protein-bound iodine concentration were at lower levels than those generally found in pituitary myxoedema or spontaneous panhypopituitarism, presumably because in these conditions pituitary function is not generally lost so completely as after surgical hypophysectomy.

A. Gordon Beckett

403. The Metabolism of Iodine in the Thyroid Gland. [Review Article]
I. P. C. Murray, M. J. Spiro, and J. B. Stanbury. Journal of Chronic Diseases [J. chron. Dis.] 14, 473-483, Nov., 1961. 2 figs., bibliography.

ADRENAL GLANDS

404. Primary Aldosteronism: the Value of Spironolactone in Diagnosis

J. D. K. North, F. H. Sims, and E. G. SAYERS. *Lancet* [Lancer]. 2, 618-621, Sept. 16, 1961. 1 fig., 22 refs.

The authors describe a female patient who first came under observation at Auckland Hospital, New Zealand, in 1952 at the age of 36 and was then diagnosed as suffering from potassium deficiency of renal origin; she had been kept in fair health for 8 years by taking 8 to 12 g. of potassium chloride daily. In 1960 the potassium treatment was stopped and thereupon the serum potassium level fell from 4 to 2.7 mEq. per litre, while renal function was almost normal, though there was some impairment of ability to excrete acid urine and also of glucose tolerance. An intravenous pyelogram and retroperitoneal insufflation of air suggested the possible presence of adrenal enlargement and a balance study under spironolactone treatment was therefore performed, in which, while on a daily dietary intake of 90 mEq. of sodium and 76 mEq. of potassium supplemented by 40 mEg. of potassium as the chloride, 1,200 mg. of spironolactone was given daily for 4 days. During this treatment the urinary potassium output fell progressively and the urinary sodium: potassium ratio rose from about unity to nearly 4:1.

On the basis of these findings the patient was subjected to operation at which a small adrenal adenoma was found and removed. After operation she required no more potassium supplements, and a repetition of the spironolactone test provoked no alteration in either the urinary potassium output or the sodium: potassium ratio. Previously reported cases of the use of spironolactone in the diagnosis of primary aldosteronism are reviewed and tabulated for comparison.

Peter C. Williams

405. Useful Parameters in the Diagnosis of Primary Aldosteronism

E. G. BIGLIERI, P. E. SLATON JR., and P. H. FORSHAM. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 19-22, Oct. 7, 1961. 2 figs., 17 refs.

At the University of California Medical School, San Francisco, the plasma volume, urinary aldosterone excretion, and serum and urinary sodium and potassium levels were determined in 9 patients who were kept on a constant metabolic balance diet with a sodium intake calculated to be between 9 and 15 mEq. per 24 hours; 5 of the patients had primary aldosteronism, 2 hypertension, and 2 were normotensive. All 5 patients with primary aldosteronism were also hypertensive, but differed from the 2 patients with hypertension in having a low serum potassium level and a high rate of urinary aldosterone excretion. However, patients with malignant hypertension sometimes show increased aldosterone secretion and hypokalaemia and it is therefore important to exclude the possibility of primary aldosteronism in such patients.

In the present tests, when 1 g. of spironolactone was given in 4 divided doses daily for 3 days, the patients with primary aldosteronism showed a marked rise in the serum potassium level, a sodium diuresis, and a decrease in urinary potassium excretion, while the urinary aldosterone content increased above its already high levels. In the hypertensive and normotensive patients spironolactone produced only inconsiderable changes in serum potassium levels. Withdrawal of dietary sodium resulted in a prompt fall in urinary potassium excretion in the patients with primary aldosteronism, but no change in the normotensive and hypotensive patients. In all 5 patients with primary aldosteronism the plasma volume was raised, whereas the hypertensive and normotensive patients had normal plasma volumes. It is suggested that considerable help in the differential diagnosis of primary aldosteronism can be obtained by determination of the plasma volume and observation of the effect of spironolactone on the serum potassium levels.

P. A. Nasmyth

DIABETES MELLITUS

406. Calibration of a Simplified Cortisone Glucose Tolerance Test

C. R. KLIMT, F. W. WOLFF, C. SILVERMAN, and J. CONANT. *Diabetes* [*Diabetes*] 10, 351–366, Sept.-Oct., 1961. 14 figs., 12 refs.

The cortisone–glucose tolerance (C.G.T.) test as performed in this study at Johns Hopkins Hospital, Baltimore, consisted of a single dose of cortisone (50 mg. per sq. metre body surface, equivalent to about 100 mg. for an average adult male) given 1 to 5 hours before loading with glucose in a dosage of 30 g. per sq. metre. Capillary blood samples were taken before ingestion of the glucose and at hourly intervals thereafter for 3 hours, the blood glucose level being estimated by the "glucostat" micromethod. A preliminary study on 116 normal volunteer subjects showed the frequency distribution of blood glucose values to be unimodal, with the mode at 1 hour after

ingestion and positively skewed thereafter; no objective dividing line between normal and abnormal individuals was found. The test was shown to give similar repeat results in the same individual, and the blood glucose value after 1 hour was the most efficient for screening for diabetes.

A statistical analysis of the C.G.T. test results and of those of the ordinary glucose tolerance test without cortisone showed a significant correlation between the two and indicated that both tests measured the same metabolic characteristics. The C.G.T. test gives higher glucose values after glucose ingestion and also shows a greater range than the ordinary test, thus giving greater opportunity for discerning abnormality. The mean glucose values in the C.G.T. test were 3 to 11 mg. per 100 ml. higher for females than males, these differences in the fasting values and at 3 hours (but not at 1 and 2 hours) after glucose being highly significant.

The authors consider that the test is sufficiently reliable for use in a field study of genetic patterns in prediabetics.

F. W. Chattaway

407.— A Non-atheromatous Proliferative Vascular Lesion of the Retina in Diabetes Mellitus: Role in the Etiology of Diabetic Retinopathy

H. T. Blumenthal, M. Alex, and S. Goldenberg. *American Journal of Medicine [Amer. J. Med.*] 31, 382-396, Sept., 1961. 17 figs., bibliography.

From St. Louis University and the Jewish Hospital, St. Louis, Missouri, the authors describe a histological study of the vascular lesions in the retina of 84 eyes removed at necropsy, 34 being from diabetic patients and 50 from non-diabetics. Of the former patients 5 were under the age of 50, 20 were male, 28 were hypertensive, and all had been treated with insulin; of the 50 non-diabetics 11 were under the age of 50, 29 were male, and 31 were hypertensive. After fixation in 10% formalin the eyes were mounted in paraffin, sectioned, and stained by a variety of methods which are described in detail.

Inflammatory vascular lesions of the retina were found to be 15 times more common in the diabetic subjects than in the non-diabetics. Thrombotic lesions were rare in both groups of eyes, and there was no significant difference between the occurrence of atheromatous lesions in the two groups. Haemodynamic lesions were more common in the hypertensive members of both groups; in the younger diabetic patients these lesions were 2 to 3 times more frequent than among young nondiabetics, but the incidence of hypertension was higher among the younger diabetics. In the younger diabetics proliferative vascular lesions were 9 times more frequent than in young non-diabetics, while in the older diabetic patients they were 3.5 times more frequent. In regard to non-vascular exudative lesions, "cotton wool" patches were rare in both groups, while hard, waxy exudates were found only in diabetics and were almost always associated with proliferative vascular lesions. In discussing these findings the authors suggest that the proliferative vascular lesions in diabetes may be produced by an immunogenic mechanism. Charles Rolland

The Rheumatic Diseases

408. Increase of Plasma Volume in Rheumatic Fever: Its Effect on Serum Protein Pattern and Erythrocyte Count. [In English]

M. MILTENYI. Annales paediatrici [Ann. paediat. (Basel)] 197, 229-236, 1961. 1 fig., 15 refs.

The author of this paper from the University Medical School, Budapest, draws attention to the lack of quantitative data concerning the serum protein pattern in acute rheumatic fever. He determined the total quantity of circulating proteins by estimating the percentage in the plasma and the volume of the plasma. Electrophoretic fractionation of the plasma proteins then made it possible to compare the quantity of the circulating albumin and different globulins. These values were determined serially in 15 children suffering from acute rheumatic fever. The absolute quantity of circulating globulins was found to be increased. As a consequence, the plasma volume increased while the total amount of albumin and the total number of erythrocytes remained unchanged. This haemodilution is considered to be the cause of the anaemia and hypoalbuminaemia which are well recognized features of rheumatic fever.

[A great deal of work and a lot of data are skilfully compressed into very few pages of text and tables.]

John Lorber

409. Antibody to Thyroglobulin in Patients with Collagen Diseases

J. R. ANDERSON, R. B. GOUDIE, K. G. GRAY, and W. W. BUCHANAN. Scottish Medical Journal [Scot. med. J.] 6, 449–456, Oct., 1961. 39 refs.

In this study from the University and Western Infirmary, Glasgow, the antithyroglobulin antibody titres (estimated by Boyden's tanned erythrocyte agglutination technique) in a series of 127 patients with collagen diseases are compared with those in 175 control patients with various conditions whose serum was submitted for blood grouping. Sera giving a positive response were subjected to precipitation tests by the Ouchterlony method, but only 4 gave a reaction (2 from patients with Sjögren's disease and 2 from controls; 3 of the 4 had thyroid disease). All positive agglutination reactions were inhibited by thyroglobulin, but not by pooled γ globulin.

A higher incidence of positive reactions was found in the series with collagen diseases than in the controls, the proportions being 27% and 12% respectively (P<0.01 using Yates's modification of the χ^2 test). This increase in incidence is analysed according to age and sex and also in individual disease entities, selected control subjects matched for age and sex being used for this last purpose. There was a significant increase in positivity among 62 cases of rheumatoid arthritis, 26 cases of Sjögren's disease, and 17 cases of systemic lupus erythematosus, which gave positive results in 24, 38, and 35%

of cases respectively. One patient out of 16 with discoid lupus, one out of 5 with scleroderma, and one with dermatomyositis also gave positive results.

The mechanisms of autoantibody formation are discussed and the conclusion is reached that an intrinsic abnormality of the immunity system may be an additional factor in the development of thyroid autoantibodies, particularly in patients who show evidence of other autoimmune phenomena. [However, no attempt is made to relate thyroglobulin antibody to the presence or absence of rheumatoid factor or of the L.E. cell phenomenon, which was present in only 13 of the 17 cases of systemic lupus erythematosus.]

E. G. L. Bywaters

RHEUMATOID ARTHRITIS

410. Serologic Methods Employing F-II Reactant as an Aid to Diagnosis of Rheumatoid Arthritis D. S. HOWELL, P. P. VAUGHN, and B. L. BROOME. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 368–377, Aug., 1961. 1 fig., 32 refs.

Among the host of different techniques being developed for agglutination reactions for the rheumatoid factor this study from the University of Alabama Medical Center and Veterans Administration Hospital, Birmingham, Alabama, describes an evaluation of the sensitivity and specificity of a further variation of Hall's modification of the inhibition test for the detection of FII agglutinating factors. The inhibition test of Ziff elevated the sensitivity of the sheep-cell agglutination technique to 98% positivity, but remains too laborious and timeconsuming for routine use. Hall's method is simpler to perform, but still requires a 48-hour dialysis period in the preparation of the euglobulin extract. By the use of a hydrochloric acid euglobulin fractionation procedure the present authors have reduced this step to 11 hours.

Sera were examined simultaneously by this modification of Hall's method, the FII sheep-cell test of Heller, the latex fixation test of Singer and Plotz, the direct euglobulin test, and the macroscopic slide test with Hyland reagents. In all, 641 sera were tested. In 100 cases of definite rheumatoid arthritis the 5 tests gave 98, 85, 84, 95, and 98% positive results respectively. Whereas the sensitivity of the Hyland slide test was equal to that of the authors' modification, the former gave 15% positive results in non-rheumatoid cases compared with only 2.5% with the latter. In a group of 27 patients with definite rheumatoid arthritis of less than 14 months' duration a high degree of positivity (78 to 82%) was obtained with the euglobulin tests compared with 52% with the latex fixation test. No difference in the specificity of the tests was noted in a group of 104 cases of special diseases; among 43 cases of hepatic disorders

there were 14 positive results and among 22 of peptic ulcer there were 3 positive results, while cases of influenza and mumps gave no positive results.

It is concluded that the reduced time for euglobulin fractionation has proved advantageous, while maintaining a comparable satisfactory degree of specificity and sensitivity for rheumatoid arthritis.

Harry Coke

411. Interpretation of the Significance of a Positive Sensitized Sheep Cell Agglutination Test in the Differential Diagnosis of Rheumatic Disorders

N. A. HINTON and H. G. KELLY. 'Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 638-643, Sept. 9, 1961. 2 figs., 17 refs.

An evaluation to determine the significance of the results of the sensitized sheep-cell agglutination test was carried out on a group of 1,012 patients drawn from an arthritis out-patient clinic, from private practice, and from the wards of Kingston General Hospital, Ontario. The test utilized the euglobulin fraction isolated by dilution with 0.0027 N hydrochloric acid. The group included 217 cases of definite rheumatoid arthritis, 59 of possible or probable rheumatoid arthritis, and 736 cases of other rheumatic disorders. Definite rheumatoid arthritis stood out as having not only the highest incidence of positive reactions, but also a distribution of significantly higher titres than any other group.

Definition of a "false positive reaction", especially in a sensitive test such as this, is discussed. A positive reaction indicates the presence of a reacting macroglobulin which cannot as yet be differentiated into specific forms or specifically related to individual diseases. When positive reactions are obtained with non-rheumatoid diseases such as viral infections the titre tends to fall and the reaction remains positive only so long as the pathological processes concerned are active. The authors suggest that the concept should be discarded that a positive test result is specific for rheumatoid arthritis and that the result should be considered in relation to the fotal clinical picture. In this respect they grant relatively high priority (in terms of the diagnosis of rheumatoid arthritis) to high-titre positive reactions, the persistence or rise of positivity for weeks or months, and fulfilment of the diagnostic clinical criteria of the American Rheumatism Association. Details of the reactions in the various clinical groups are given [without, however, relation to specific clinical features such as the presence or absence of nodules.] Harry Coke

412. Epidemiology of the Sheep Cell Agglutination Test J. Ball and J. S. Lawrence. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 235-243, Sept., 1961. 4 figs., 21 refs.

In recent years the authors, working at the Rheumatism Research Centre, University of Manchester, have studied seven different population samples drawn from Leigh (Lancashire), Glamorgan and Rhondda (Wales), Wensleydale (Yorkshire), Annandale (Scotland), Rotterdam (Netherlands), and Heinola (Finland) and in the present paper they report the results of the sensitized sheep cell test in these populations. In order to minimize secular

errors the sensitivity of the test was standardized against a series of human sera of known agglutinating activity.

The prevalence of positive titres in the sheep cell agglutination (S.C.A.) test varied between 1.6 and 5.4% in the different population samples in subjects aged 55 to 64 years, being significantly more frequent in urban than in rural subjects; in both urban and rural samples. however, the proportion of positive reactors was similar in males and in females. When all age groups over 15 years were studied positive results in the S.C.A. test were equally distributed between males and females in an urban sample, but in a single rural sample positive reactions were obtained more frequently in females than in males. The frequency of positive tests increased with age in two urban samples, but in one rural sample this occurred in females but not in the males. In first-degree relatives of 261 members of an urban population positive titres were obtained in 3% of the relatives of propositi with a negative titre and in 12% of relatives of propositi with a positive titre. Positive tests were not found more frequently than would be expected by chance in both husband and wife, from which it is concluded that genetic rather than environmental factors are responsible for the observed familial aggregation of positive titres. Of particular interest was the fact that only about 20% of these seropositive individuals presented evidence of rheumatoid arthritis as defined by the criteria of the American Rheumatism Association. B. M. Ansell

413. The Frequency Distribution of Episodes of Rheumatold Arthritis as Shown by Periodic Examination G. Beall and S. Cobb. *Journal of Chronic Diseases [J. chron. Dis.*] 14, 291–310, Sept., 1961. 2 figs., 12 refs.

From observations made monthly on a group of 274 employed men the severity gradient of rheumatoid arthritis among them has been described in terms of the part! of their time that they spend with active disease. This frequency distribution is reasonably well represented by a Pearson Type I function. The Type I frequency distribution can be found from an initial determination of whether a man is in episode, plus a subsequent redetermination for each man not then in episode.

The method developed provides a simple approach to making comparisons of the frequency of rheumatoid arthritis between groups in such a way as to eliminate the uncertainties arising from simple point prevalence measurements. Essentially, the procedure we recommend suggests that the usual point prevalence survey be supplemented by at least one additional examination to see how many additional afflicted persons are found. The second examination is curiously productive in that the two examinations are sufficient to specify the entire situation, if one is satisfied to assume the Type I distribution. Further examinations make it possible to check this point.

From the point of view of immediate results, we have a new view of rheumatoid arthritis as a very common disease that is only occasionally disabling. This position is supported by both data and theory which show how many cases with symptoms of rheumatoid arthritis will be disclosed by long-continued examination. The evidence of these several rheumatoid manifestations suggests that the older notion of a distinct separation between rheumatoid arthritis and fibrositis is probably unwarranted; the continuity of affliction dispels this. The notion now must be that we are dealing with a single continuous gradient of disease from no involvement to severe involvement. The mathematical techniques presented are presumably applicable to the study of other remittent diseases.—[Authors' summary.]

414. Treatment of Rheumatoid Arthritis by Intramuscular Triamcinolone Acetonide and Triamcinolone Diacetate J. ZUCKNER. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 274–280, Sept., 1961. 6 refs.

Having observed that after intra-articular injection of 100 mg. of triamcinolone acetonide or triamcinolone diacetate there were systemic effects with a generalized anti-inflammatory response, the author tried intramuscular injections of these drugs in 36 patients with rheumatoid arthritis at the University of St. Louis Hospital, Missouri, the total number of injections being 112. Acetonide was given in 68 injections and the diacetate in 44, the dose of each drug being 100 mg. Of the 36 patients 26 also received corticosteroids by mouth and 28 were receiving gold salts. The duration of the observation varied; 17 patients were observed for 100 or more days, 6 of them for one year; the remaining 19 were each observed for an average period of 70 days. The results of this treatment were compared with those obtained in the same patients with intramuscular injection of 100 mg. or 500 mg. of hydrocortisone acetate.

Analysis of the results showed that 73% of the injections of either the acetonide or the diacetate of triamcinolone were followed by improvement; this lasted for an average of 20.2 days after injection of the former compound and 16.2 days after the latter. The average duration of improvement after injection of 500 mg. of hydrocortisone acetate was 5.2 days. The side-effects were in general similar to those of corticosteroids given by mouth, but the author advises a long-term study before any conclusions can be drawn. Possible explanations of the improved results from this treatment are discussed.

K. C. Robinson

415. Pitultary Corticotrophin (ACTH) Production in Rheumatoid Arthritis Tested Indirectly with Metopiron (Su 4885)

J. L. KALLIOMÄKI, N. T. KÄRKI, H. A. SAARIMAA, and E. TALA. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 244-246, Sept., 1961. 8 refs.

This short paper from the University of Turku, Finland, reports the results of the inhibition of 11- β -hydroxylation in the adrenal cortex by the use of "metopiron" (Su 4885) in 10 patients suffering from rheumatoid arthritis, none of whom had received steroid therapy for at least one year, and in a control group of 10 patients suffering from various other disorders. During the 6-day study, days 1 and 2 and 5 and 6 were used as control days, while metopiron was given orally in a dosage of 500 mg. 6-hourly on days 3 and 4, the urine being collected for each 24 hours and analysed for total 17-hydroxycorti-

costeroid content. In the rheumatic patients the response of the pituitary gland to metopiron, that is, the production of ACTH, did not differ from that in the controls, although there was a tendency for the response to be delayed by about a day in the rheumatoid group.

B. M. Ansell

416. Sacro-lliac Joint in Adult Rheumatoid Arthritis and Psoriatic Arthropathy

A. St. J. DIXON and E. LIENCE. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 247-257, Sept., 1961. 7 figs., 6 refs.

Early and constant signs of ankylosing spondylitis are radiological changes in the sacro-iliac joints, but similar changes may be seen in some cases of rheumatoid arthritis. The radiological appearances of these joints vary with age, sex, and the technique employed. To determine the true incidence of sacro-iliitis in rheumatoid arthritis a controlled study was carried out at Hammersmith Hospital, London, and for this purpose radiographs were examined as follows: 56 from patients with rheumatoid arthritis giving a positive response to the differential agglutination test (D.A.T.) and 56 from matched controls; 40 from patients with rheumatoid arthritis giving a negative response to the D.A.T. and from 40 matched controls; 33 from patients with psoriasis and arthritis and 33 controls; and 36 from patients with ankylosing spondylitis. Each radiograph was read three times for each of the following characteristics: erosions, sclerosis, narrowing, and widening. Attention was mainly directed to the synovial joint, which occupies the lower half of the joint space.

Only 74 out of 112 joints of the patients with classic rheumatoid arthritis were entirely normal, compared with 106 out of 112 joints of controls. Narrowing was observed in some of the rheumatoid joints, the degree of narrowing appearing to increase with the age of the patient and probably also with the duration of the disease. The joints in D.A.T.-negative patients with rheumatoid arthritis did not differ significantly from those of the controls, but in the patients with psoriasis there was an increased frequency of narrowing or fusion. There was narrowing or fusion in a high proportion of patients with ankylosing spondylitis; in this group there were various additional signs not observed in the other diagnostic groups, including gross widening in early cases and "ghost joints", "stars" and the "dagger sign" in late cases.

The authors' observations confirm the view that the sacro-iliac joints may occasionally be affected in rheumatoid arthritis but that changes, when they do occur, consist mainly of narrowing and are seen chiefly in older patients with long-standing disease. In none of the cases did the appearances closely resemble those of ankylosing spondylitis.

K. C. Robinson

417. Effect of Heat on the Rheumatoid Factor Precipitation Reaction with Human Gamma-globulin
W. V. Epstein and M. Ross. Arthritis and Rheumatism
[Arthr. and Rheum.] 4, 480–489, Oct., 1961. 3 figs., 27

GOUTY ARTHRITIS

418. Uricosuric Effects of Probenecid and Zoxazolamine in Gout: a Comparative Study

J. V. RIVERA. Archives of Internal Medicine [Arch. intern. Med.] 108, 512-518, Oct., 1961. 25 refs.

It is well established that agents which control hyperuricaemia beneficially affect the joint manifestations of gout and bring about a reduction in the size of tophi. Probenecid, which is generally considered to be the most satisfactory drug for prolonged treatment, was used as a standard for comparison of the effects of a newer agent, zoxazolamine, a muscle relaxant with a potent uricosuric action

At San Patricis Veterans Administration Hospital, San Juan, Puerto Rico, 30 patients in whom the diagnosis of gout was established were assigned at random to one of two treatment groups—probenecid in a dosage of 1.5 g. daily or zoxazolamine 1.5 g. daily; after the first few days the dosage of zoxazolamine was reduced in most of the patients to 0.25 g. twice daily.

The fall in the serum uric acid level which occurred after treatment for one day and 3 days was significantly more rapid when 1.5 g. of zoxazolamine was given daily than when the same dosage of probenecid or 0.5 g. daily of zoxazolamine was administered. The effect of 0.5 g. daily of zoxazolamine on the serum uric acid level and on the uric acid clearance rate was similar to that of 1.5 g. of probenecid daily. Minor gastric discomfort occurred in 2 patients in each group and a drug rash was observed in 2 patients receiving zoxazolamine and one receiving probenecid. During the first day of treatment with 1.5 g. of zoxazolamine acute pain suggesting a renal or ureteric origin-lieveloped in 5 patients, none of whom passed a recognizable calculus. It is suggested that because pain occurred on the day of maximum uricosuria and abated quickly in spite of continued treatment, it was probably due to crystallization of uric acid in the kidneys. No similar reaction was observed in any of the patients given 0.5 g. of zoxazolamine daily.

Probenecid is considered to be a very safe drug. Toxic reactions from zoxazolamine when used as a muscle relaxant have been infrequent, although serious complications have been reported. The author concludes that the clinical choice of drug will be guided by considerations other than the difference in unicosuric activity.

Kenneth Stone

419. Efficacy of Colchicine Prophylaxis in Gout: Prevention of Recurrent Gouty Arthritis Over a Mean Period of Five Years in 208 Gouty Subjects

Ts'AI FAN YÜ and A. B. GUTMAN. Annals of Internal Medicine [Ann. intern. Med.] 55, 179-192, Aug., 1961. 1 fig., 23 refs.

Until comparatively recently there has been only an occasional reference in the literature to the regular use of small (suppressive) doses of colchicine as a prophylactic measure against acute gouty arthritis. In a preliminary study of the pattern of acute attacks unmodified by prophylactic measures it was found that about three-

quarters of a series of 614 patients who could reliably recall the onset of their first attacks had a second seizure within 2 years of the first; in the remaining patients, however, this interval was very variable. In 506 of the cases the number of recurrences and the history were precise enough to discern a pattern of frequency and severity. It was found that in 47% there was the classic course of increased frequency of attacks, in 34% there was a relatively constant number of attacks year after year, and in 17% there was no consistent pattern. In the remaining 2% the attacks decreased in frequency with time. Attacks, as judged by the disability involved, became increasingly severe with time in 24%, were of constant severity in 56%, and were so variable in intensity as to form no regular pattern in 12%. In 8% attacks became less severe, usually as the result of prompt treatment.

Colchicine was tried in 208 patients (including 8 females) who had had regular acute seizures of gout, classified as "severe" or "moderately severe", for a period of years. The drug was given daily for at least 2 years, the average period of observation being 5.4 years. Tophi were seen in 95 of these patients at the start of the regimen and appeared in 17 further patients during the period of observation. Stiffness, pain, and tophaceous involvement of joints indicative of chronic gouty arthritis were noted in 49 patients. The initial dosage of colchicine was 1 mg. daily, and this was maintained throughout in 138 cases. In 45 cases the daily dose was later reduced to 0.5 mg. or less, but in 18 cases 1.5 to 2.0 mg. daily was required. Minor bowel disturbances occurred at the onset of treatment in 4% of the patients, but tolerance was established by graduating the dosage or by giving the drug in enteric-coated capsules. Extra doses (2 to 3 mg. daily) were given to abort incipient attacks. Chlorothiazide and other drugs tending to incite acute seizures were, if possible, withdrawn, and uricosuric drugs were discontinued at the start of the regimen if the patient had frequent and severe acute attacks. Uricosúric drugs were later given, in addition to the colchicine, to 89 patients.

As a result of this prophylaxis 110 patients became virtually free from attacks and a further 72 had only mild episodes. In 26 patients there were still appreciable symptoms, but many of these patients were young, with disease that was fulminant or was complicated by other factors. No real difference was observed between the group given colchicine alone and the group given colchicine alone and the group given colchicine and uricosuric drugs. [These results relate exclusively to the incidence and severity of attacks.] Apart from bowel sensitivity in a few cases no side-effects of colchicine were encountered. The possibility of genetic consequences is considered, but there was no evidence of these in the present series.

The authors consider that colchicine is effective andreasonably safe and is probably preferable to prolonged
daily administration of phenylbutazone. They emphasize that the prophylactic regimen described does not
prevent the formation of tophi, for which uricosuric
agents must be given. It is their practice to withhold
the latter drugs until there are symptoms or signs of
tophaceous deposits.

B. E. W. Mace

Physical Medicine.

420. Electromyographic Studies in Myopathles and Related Conditions

M. A. Perlstein, M. Turner, and H. Elam. Archives of Physical Medicine and Rehabilitation [Arch. phys. Med.] 42, 447-457, June, 1961. 3 figs., 13 refs.

The results are reported from Cook County Hospital, Chicago, of electromyographic (EMG) studies on 33 patients with muscular dystrophy, 11 with severe sequelae of poliomyelitis, and 9 with cerebral palsy. In all cases studies were carried out with monopolar and concentric bipolar needle electrodes, connected to either a "meditron," electromyograph or a Grass Model P 4 pre-amplifier with Du Mont dual-beam oscilloscope. both photographic and tape recordings being made. In every patient the gastrocnemius, rectus femoris, deltoid, and biceps brachii muscles were tested, often bilaterally, together with one of the other most involved muscles and one of the least involved muscles. Several electrodes were inserted in each muscle and readings taken at rest, on weak volition, and strong volition. The criteria of normal and abnormal potentials are given, and wefe as widely accepted.

Normal findings were obtained in all 9 patients with cerebral palsy. The patients with poliomyelitis showed typical findings of lower motor neurone damage, namely, fibrillation at rest and polyphasic potentials on volition, and in a few cases giant potentials. Of the 33 with muscular dystrophy 30 showed dystrophic potentials on volition, 11 polyphasic potentials, and 11 myotonic potentials, but there were some characteristic findings with each clinical type; thus in 18 out of 20 patients with pseudohypertrophic muscular dystrophy there was electrical silence at rest, fibrillation being present in the other 2. Dystrophic potentials were present in 19 out of 20, and 11 showed myotonic activity. The 4 patients with facio-scapulo-humeral muscular dýstrophy showed dystrophic potentials and only one showed fibrillation. "Of 9 patients with amyotonia congenita 4 had fibrillation potentials, 7 dystrophic potentials, and one giant poten-J. B. Millard : tials.

421. Isometric Exercises in the Paraplegic and in the Patient with Weakness of Quadriceps and Hamstrings

J. W. GERSTEN. Archives of Physical Medicine and Rehabilitation [Arch. Phys. Med.] 42, 498-506, July, 1961-6 figs., 14 refs.

In this paper from the University of Colorado School of Medicine and Craig Rehabilitation Center, Lakewood, Colorado, an investigation is described of the value, respectively, of isotonic and isometric exercises in increasing muscle function. The author states that anoxia is not important. Tension was recorded with a cable tensiometer using the 10-repetition maximum as a standard technique and triceps muscle activity on the electromyograph. The knee muscles were studied in patients

with hip and knee disabilities and the elbow muscles in paraplegic patients. Isometric exercises were given to one limb and isotonic progressive resistance exercises to the contralateral limb once or twice a day 5 days a week. The progressive resistance routine was 10 warm-up contractions at one-half maximum, then 10 contractions at a maximal level at a rate of 15 per minute. The isometric exercises consisted of 5 maximal contractions lasting 5 seconds with 5-second rest periods, intervening and no warm-up period.

Before this investigation none of the paraplegic patients had had any significant exercises and other exercises were restricted except in one group of patients who had unlimited exercises after 4 weeks. Improvement in muscle function was essentially the same after both isotonic and isometric exercises. No cross effects were noted. The triceps muscles showed a greater increase in strength than the quadriceps muscles. It would appear that in order to increase muscle strength exercises are necessary and the best are those which the patient can carry out according to his disability.

J. B. Millard

422. The Basis of Prophylaxis against Disease in Athletics. (Основные пути профилактики заболеваний у спортеменов)

А. G. DEMBO. Советская Медицина [Sovetsk. Med.] 25, 67-72, Sept., 1961. 10 refs.

One of the problems under review at the Experimental Institute of Physical Culture, Leningrad, is the morbidity. among sportsmen and athletes and the means of lowering its incidence. Illness in such subjects may be (1) extraneous, that is, not in any way related to their training or athletic activities; or (2) directly due either to incorrect methods of training or to intensive training while they are suffering from subacute or chronic sepsis or undergoing mental strain, such as working for examinations.

Intensive training for athletics and other strenuous competitive contests may make manifest a physical (for example, cardiac) or psychological weakness which under ordinary conditions would cause no symptoms. Subjects, therefore, who are about to prepare for such strenuous activities should be carefully examined by expert physicians, armed with the latest apparatus and instruments for diagnosis; before entering on their intensive training. Strenuous contests should not be undertaken during periods of study for critical examinations or other forms of mental strain, to which highly-trained athletes are particularly vulnerable, nor too soon after any infectious disease. Foci of infection, such as carious teeth or septic tonsils, should be eliminated before intensive training for sport is undertaken, and no such. training should be entered upon unless an experienced doctor has passed the athlete as fit to undergo it. Such! prophylactic care has been successful in substantially reducing morbidity in athletes. L. Firman-Edwards

Neurology and Neurosurgery

423. Effect of Intravenous Urea on the EEG of Brain Tumor Patients

D. SILVERMAN, S. PARANDIAN, and H. SHENKIN. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 587-590, Aug., 1961. 3 figs., 8 refs.

At the Episcopal Hospital, Philadelphia, each of 6 patients with a verified cerebral tumour was given 90 g. of urea in 210 ml. of 10% dextrose solution intravenously over a period of 70 to 80 minutes and the electroencephalogram (EEG) then recorded continuously during and for 1 to 3 hours after the infusion. In all cases there was a reduction in both generalized and particularly focal theta and delta activity, together with a slight increase in the amount of fast activity. The effect began 20 to 30 minutes after the start of the infusion of urea, reached its maximum in 70 to 100 minutes, and then slowly diminished; in one patient the EEG became normal. Corresponding with the improvement in the EEG a marked fall in the level of the pressure in the cerebrospinal fluid was noted.

The technique has not yet been used in cases in which focal slow activity is completely obscured by the generalized abnormalities. The authors conclude that the effects observed were due to reduction of the oedema around the tumour.

L. G. Kiloh

424. Electro-clinical Correlation in the Positive Spike Phenomenon

J. R. HUOHES, D. GIANTURCO, and W. STEIN. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 599-605, Aug., 1961. 13 refs.

There have been few reported studies giving a systemic account of the electro-clinical correlations in patients showing the positive-spike phenomenon in the electroencephalogram (EEG). At the University, of Buffalo Medical School, New York, the authors have therefore studied 115 patients showing positive spikes at 7 and 14 per second in their sleep EEGs recorded with a monopolar montage, and have collated the results with the details of the patients' clinical histories and of their waking EEGs, including the responses to hyperventilation and photic stimulation. The ages of these 81 male and 34 female patients ranged from 3 to 42 (mean 15.5) years, 44 of them being aged between 13 and 15 years. A history of postictal head injury was obtained in 46 cases [but the nature and severity of these injuries is not indicated]. Disturbed behaviour, often impulsive and aggressive in character, was shown by 71 of the patients and there was evidence of autonomic dysfunction in 76; either or both of these states occurred in a total of 104 cases. Autonomic dysfunction was manifested by headache, abdominal pain, vertigo, dizziness, "blackouts" or faints, nausea and vomiting, obesity, sweating, chest

pain, or enuresis. A history of "epileptiform disorders" was obtained in 31 cases.

The 7- and 14-per-second positive spikes were usually bilateral, and if unilateral were more likely to be confined to the right side. Posterior temporal slow activity was frequently present in these cases, with corresponding lateralization. As compared with the EEGs of patients with similar histories but not showing positive spikes, the waking EEGs of these patients with spikes tended to show a background rhythm of lower frequency, more posterior temporal slow activity, more epileptiform sharp waves, more "build-up" with hyperventilation, and poorer photic driving. Although in their discussion the authors conclude that the appearance of positive spikes in the EEG constitutes an epileptiform phenomenon they leave open the question whether or not the clinical phenomena shown by these patients are epileptic, noting that "the definition of clinical epilepsy has changed throughout the years ". L. G. Kiloh

425. Echoencephalography. IV. The Midline Echo; an Evaluation of its Usefulness for Diagnosing Intracranial Expansivities and an Investigation into its Sources. [Monograph, in English]

S. Jeppsson. Acta chirurgica Scandinavica [Acta chir. scand.] Suppl. 272, 1-151, 1961. Bibliography.

HEREDITARY AND CONGENITAL DISEASES

426. Anencephalus in Scotland

R. G. RECORD. British Journal of Preventive and Social Medicine [Brit. J. prev. soc. Med.] 15, 93-105, July, 1961. 8 figs., 13 refs.

This report from the University of Birmingham is concerned with the search for causal factors in the aetiology of anencephalus. Because the disease is rarely compatible with life a useful method of approach was considered to be the study of a large series of stillbirths having anencephalus as the stated or probable cause. From 1939, when the Registration of Stillbirths Act (Scotland) became effective and required a statement as to the cause of every stillbirth registered, the annual returns of the Registrar-General for Scotland provide information on such a series, and these, supplemented by additional information concerning the age and parity of the mother, month of birth, and social class for the years 1949 to 1958, supplied by courtesy of the Registrar-General, form the data of this study.

Anencephalic stillbirth rates were lowest for mothers aged 25 to 29 and this was generally true for all parities, even for second births, in which group the lowest rates occurred whatever the age of the mother. Thus the incidence of anencephalus varied with both parity and

age, but independently. The rates also showed a steep social-class gradient, being four times as high in Social Class V as in Social Class I, but standardization for social-class differences produced little change in the age-parity rates. It was also demonstrated that the high incidence of anencephalus in the final 5 years of the series (1954 to 1958) was present in every maternal age group, every parity group, in each social class, and at each season of the year. After making allowance for the fact that the period of gestation in a proportion of anencephalic stillbirths is shorter than normal, a consistent pattern of variation with season of the year was also apparent for every parity group and for each social class. The incidence of anencephalus was highest amongst births occurring during the trimester November to January and lowest amongst those occurring in May to July—a finding in sharp contrast to the seasonal distribution of all births (live and still) in Birmingham in 1950, where the lowest proportion of births occurred in November to January.

On the assumption that any causal factor must have operated about eight months before the termination of these pregnancies, if they had gone to term, the author argues that such a factor must have been most effective from March to July (8 months before the trimester November to January, when the incidence was highest) and least effective from September to January. These periods of high and low intensity corresponded well with the months which had many and few hours of daylight and sunshine and to a lesser degree with those of high and low air temperature. They did not coincide, however, with the months when notification of the common infectious diseases and influenza were high and low. An exception to this was rubella "but this is presumably a chance association because the teratogenic effects of rubella have been thoroughly investigated and there is no evidence that it causes anencephalus"

After discussing the pros and cons of other hypotheses which might explain the findings the author concludes "that several factors are probably involved in the aetiology of anencephalus, but that much of the present evidence would be consistent with an infective agent as the cause. There is less evidence to support a nutritional hypothesis".

E. Lewis-Faning

427. Psychotic Episodes in the Course of Huntington's Chorea, with Particular Regard to the Formation of Delusions. (Psychosen im Verlauf der Huntingtonschen Chorea unter besonderer Berücksichtigung der Wahnbildungen)

F. STRELETZKI. Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.]-202, 202-214, 1961. 1 fig., 22 refs.

The investigation here reported from the University of Marburg is based on a collection of over 5,000 cases of Huntington's chorea, of which 1,200 were satisfactorily documented. From these the author selected the cases of 67 patients who showed marked psychotic episodes and for whom necropsy reports were available.

The psychotic episodes were not scattered randomly tracts, whereas cortical lesions we throughout the course of the illness, but tended to appear minor and relatively unimportant.

at the beginning and towards the end of the middle third of the total course. The syndromes which appeared at the beginning of the illness showed great similarities to the endogenous psychoses, particularly to schizophrenia, so that in some cases a mistaken diagnosis of schizophrenia or manic-depressive psychosis was in fact made. The clinical features of the psychoses appearing in the later part of the illness, when the organic process was quite advanced, resembled in some cases the picture of chronic schizophrenia with delusions and hallucinations, whereas in others they were more like the crude organic. psychoses similar to the classic picture of general paralysis. Many cases showed similarities to the senile psychoses. The author uses these findings to illustrate his view that the pictures presented by the endogenous and exogenous psychoses are dependent on the extent and rapidity of progress of the underlying organic lesion; a view he shares with many workers of the Gestalt school of psychiatry. J. Hoenie

... BRAIN AND MENINGES

428. Extensive Lesions in the White Matter of the Hemispheres after Closed Cerebral Trauma Producing the "Apallic" Syndrome (Parasomnia) followed by Partial Rehabilitation. (Ausgedehnte Hemisphärenmarkschädigung nach gedecktem Hirntrauma mit appallischem Syndrom und partieller Spätrehabilitation)

G. ULE, W. DÖHNER, and E. BUES. Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.] 202, 155-176, 1961. 8 figs., 21 refs.

From the University of Kiel 3 cases of severe closed head injury resulting in extensive lesions in the white matter of the hemispheres are described; 2 of these patients died and were examined post mortem. Such a condition shows three distinct phases. The initial phase, which may last weeks or months, is characterized by deep unconsciousness with decerebrate rigidity and transient extensor spasms, tetrapareses, hyperpnoca, and autonomic disturbances such as excessive salivation and hyperhidrosis. This merges by gradual transition into the second phase, which is manifested by a peculiar waking state during which the patient may lie for weeks with the eyes open, but not showing any spontaneous movement, and changing from wakefulness to sleep by an autonomic self-governing rhythm. This condition was termed "apallic" by Kretschmer, but has been described under other names such as "parasomnia" (Jefferson) or " akinetic mutism " (Cairns). The authors consider that this state results from a blocking of pathways which isolates the cerebral cortex. During this phase the tetraparesis is gradually replaced by primitive massive movements, such as the grouping reflex or sucking reflex. The electroencephalogram (EEG) shows absence of alpha waves and is dominated by generalized delta waves, while air encephalography shows enlarged ventricles. The post-mortem findings in the 2 fatal cases confirmed that there is massive degeneration and atrophy of fibre tracts, whereas cortical lesions were found to be only

If the second phase of the syndrome is survived the patient presents yet a different clinical picture, this constituting the third phase. Here fine co-ordinated and spontaneous movements return, the autonomic sleep rhythm becomes a normal night-day rhythm, and the alpha rhythm reappears in the EEG. The mental state is still grossly abnormal, with entire lack of spontaneity, but fair responsiveness to outside stimuli; there is great variability of performance, but fair preservation of affect which makes good contact with the patient possible. Although there is usually gross reduction in the lèvel of performance, the authors consider this to be due to a peculiar dissociation of individual psychic areas of activity rather than to ordinary dementia. The one surviving patient in this study remained greatly dependent on nursing supervision, but improved in response to attempts at re-education. J. Hoenig

429. A Long-term Study of Cerebral Vascular Disease S. N. GROCH, E. McDevitt, and I. S. WRIGHT. Annals of Internal Medicine [Ann. intern. Med.] 55, 358-367, Sept., 1961. 5 figs., 25 refs.

A long-term study of cerebral vascular disease, which was begun at Bellevue Hospital, New York, in 1956, included a controlled trial of anticoagulant therapy in selected cases of recent cerebrovascular disease. Of the 189 patients admitted to the trial—representing less than one-third of all patients referred for study—the majority were suffering from "completed stroke" and 92 of them received anticoagulant therapy, while 97 did not and served as a control group. Exclusion from the trial was for the following reasons: inadequate history, presence of stupor or coma, abnormal cerebrospinal fluid, severe hypertension, hepatic or renal disease, haemorrhagic disease, peptic ulcer, terminal phase of illness, impending transfer to another hospital, or death before the establishment of anticoagulant therapy. A further 10% of patients referred were excluded because anticoagulant therapy was considered obligatory on account of associated cerebral embolism or myocardial infarction. The treatment and control groups were comparable in respect of age and sex distribution, site of lesion, and presence of associated disease. Anticoagulant therapy was with dicoumarol or warfarin and was aimed at maintaining the one-stage Quick time at between 2 and 21 times the control time of 14 to 16 seconds. In spite of the difficulty in maintaining controlled anticoagulant therapy in out-patients, the patients were treated for an average period of 10 months and observed for an average of 20 months. [No detailed information on the duration of treatment and follow-up is given.]

There were 26 deaths in the treated group and 35 in the control group. Of these latter, 14 were attributed to recurrent thrombo-embolism, but no deaths due to this cause occurred in patients receiving anticoagulant therapy, although 5 of them died from recurrent strokes at a time when they were not receiving an anticoagulant drug. Non-fatal thrombo-embolic incidents likewise occurred more frequently in the control group than in the treatment group, and those which did occur in the treatment group generally did so when anticoagulant bolic rate for oxygen, and cerebral vascular resistance

therapy was inadequate or had been discontinued. On the other hand there were 20 haemorrhagic episodes in the treatment group, all necessitating cessation of therapy, and 3 of these episodes were fatal; in contrast there was only one haemorrhagic episode in the control group and this was fatal. The authors conclude that long-term anticoagulant therapy, properly maintained, can reduce the recurrence of thrombo-embolic disease in patients with a completed stroke, but they note that there is a high incidence of haemorrhagic complications and that this form of treatment is only indicated in carefully selected patients who probably form no more than onethird of all patients with cerebral vascular disease.

Bernard Isaacs

430. Serum Cholesterol Level in Cerebral Infarction A. HEYMAN, M. D. NEFZGER, and E. H. ESTES JR. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 264-268, Sept., 1961. 10 refs.

In this paper from Duke University, Durham, North Carolina, a study is reported of the serum cholesterol level in 68 men (including 21 negroes) admitted consecutively to hospital with a diagnosis of cerebral infarction caused by atherosclerosis. The mean age of the group was 60 years, 38 of the patients being in the seventh decade. The findings were compared with those in a group of 83 male patients of comparable age and race distribution, who suffered from a variety of diseases but had no evidence of coronary, cerebral, or peripheral atherosclerosis. The mean serum cholesterol level in the patients with cerebral infarction was 227 mg. per 100 ml. and that in the controls was 205 mg. per 100 ml., the difference being statistically significant. The highest serum cholesterol levels were found in men in the sixth decade, and the level thereafter declined, especially in patients with cerebral infarction. The values were not significantly affected by race or by the coexistence, in patients with cerebral infarction, of hypertension or heart disease.

It is concluded that the hypercholesterolaemia in the patients with cerebral atherosclerosis "suggests that efforts should be made in the younger patients at least to reduce the serum cholesterol in an attempt to prevent progression of the atherosclerotic process"

[It is not stated in what proportion of patients with cerebral infarction normal serum cholesterol levels were. Bernard Isaacs present.]

431. Anticoagulants and Cerebral Hemodynamics: Action of Bishydroxycoumarin

W. H. KEMPINSKY, W. R. BONIFACE, J. B. A. KEATING, and W. WEINSTEIN. Archives of Neurology [Arch. Neurol. (Chicago) 5, 275-278, Sept., 1961. 14 refs.

The authors have examined the hypothesis that the beneficial action of anticoagulant therapy in cases of carotid and vertebral-basilar artery insufficiency may be due to a general cerebral vasodilator effect of the drug, and for this purpose carried out haemodynamic studies in 10 patients suffering from clinically stable cerebral vascular disease. Cerebral blood flow, cerebral metawere measured twice in each patient—first when no treatment was being given and secondly when the prothrombin concentration had been depressed to the therapeutic range by administration of dicou marol. No significant difference was observed between the haemodynamic values before and those during anticoagulant therapy. It is concluded that these experimental data do not support the assumption that anticoagulant drugs have a general vasodilator effect.

Bernard Isaacs

432. Influence of Acetazolamide on Cerebral Blood Flow

D. L. EHRENREICH, R. A. BURNS, R. W. ALMAN, and J. F. FAZEKAS. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 227–232, Aug., 1961. 23 refs.

At the New England Center Hospital, Boston, cerebral haemodynamic studies were carried out before and after intravenous administration of acetazolamide in 10 patients with intermittent cerebral vascular insufficiency. There was a significant increase in cerebral blood flow due to a diminution in cerebral vascular resistance, this usually being more marked than that induced by inhalation of 5% carbon dioxide for 5 minutes. The changes persisted for at least one hour after administration of the drug.

Hugh Garland

433. Arm to Retina Fluorescein Appearance Time: a New Method of Diagnosis of Carotid Artery Occlusion N. J. David, Y. Saito, and A. Heyman. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 165-170, Aug., 1961. 5 figs., 9 refs.

A new diagnostic procedure for carotid artery occlusion is described in this paper from Duke University Medical Center and the Veterans Administration Hospital, Durham, North Carolina. Rapid intravenous injection of 5 ml. of 5% fluorescein is followed within a few seconds by the sudden appearance of fluorescein in the retinal vessels, which can be observed with an ordinary ophthalmoscope. Fluorescence of the retinal arteries precedes by a few seconds fluorescence of the retinal veins. Two observers are necessary and the onset of fluorescence of the arteries is recorded on stop watches. Wide dilatation of the pupils, a dark room, and a cooperative patient are essential. The test has been carried out on 11 patients with known carotid arterial occlusion and 21 control subjects. There was a "noteworthy delay" in the appearance time of the dye in the ipsilateral retinal vessels in 10 of the 11 patients with carotid occlusion. In the control group the dye appeared almost simultaneously in the two eyes. The authors consider that this procedure is safe and simple to perform and a useful diagnostic adjuvant in cerebrovascular disease.

Hugh Garland

434. Seizures in Chronic Subdurâl Hematoma M. Cole and E. Spatz. New England Journal of Medi-

cine [New Engl. J. Med.] 265, 628-631, Sept. 28, 1961. 28 refs.

Seizures are considered to be rare in cases of chronic subdural haematoma. To determine the relationship between the latter condition and convulsive seizures the

authors reviewed the data in 50 consecutive cases of chronic subdural haematoma admitted to the City Hospital, Boston, before 1960. None of these was associated with blood dyscrasia, anticoagulant therapy, or primary subarachnoid haemorrhage. In 21 cases seizures of some kind had occurred before operation. The ages of the patients ranged from 2 months to 88 years. In 8 a past history of seizures unrelated to the subdural haematoma was obtained, but in 6 of these no seizures had occurred during a preoperative stay in hospital and these 6 were included in the group of 29 patients without seizures. Seizures were the major complaint in 5 patients, of whom 3 had unilateral status epilepticus; 4 of these had multiple unilateral seizures, and one had had a single generalized seizure. Multiple unilateral seizures. were the most common type (14 cases) and in all except one case were contralateral to the haematoma. Four patients had a single seizure, 3 of which were generalized and one was unilateral. Of the 6 patients with bilateral haematomata 4 had seizures-2 a single generalized seizure, one a single unilateral seizure, and one shifting partial seizures. Brain lesions were found at operation in 13 of the 50 patients. The occurrence of seizures was not related to age, past history of convulsive disorder, or prognosis. The cerebrospinal fluid was normal in only 2 patients who had seizures.

The authors discuss the reasons for the high incidence of seizures in their patients compared with the incidence reported in the literature, and tentatively suggest that this may be related to the high percentage in their series of alcoholics suffering repeated head trauma.

R. Wyburn-Mason

435. Space Occupying Lesions in Older Patients. [In English]

J. H. A. VAN DER DRIFT and O. MAGNUS. Psychiatria, neurologia, neurochirurgia [Psychiat. Neurol. Neurochir. (Amst.)] 64, 192-201, May-June [received Oct.], 1961. 12 refs.

The clinical, electroencephalographic, angiographic and pathological findings in 3 groups of patients (under 50 years, between 50 and 60 years, and above 60 years of age) with space-occupying intracranial lesions have been compared. For the purpose of this study it proved to be necessary to make a distinction between 2 types of such lesions: "irritative" or "compensated" lesions on one hand, "destructive" or "decompensated" lesions on the other hand. The criteria for this distinction have been indicated.

In the older age groups the pathology of a space-occupying intracranial lesion in the "irritative" stage has a number of features in common with an ischaemic lesion. In correspondence with this there are often remissions in the clinical course and initially there are usually no signs of increased intracranial pressure. In the EEG the findings are often also very similar to those which are found in an ischaemia of the superficial branches of the Sylvian artery. The slowing of the circulation similar to what is found in older patients with an ischaemic lesion is often confirmed by cerebral angiography. The somewhat misleading clinical and EEG findings in older patients with a space-occupying lesion in the "irri-

tative" stage may lead to an erroneous diagnosis of an ischaemic lesion.

In the "destructive" or "decompensated" stage there are less differences between older and younger patients. The pathological investigation in older patients often shows more ischaemic disturbances in the opposite hemisphere. This usually does not give rise to clear clinical signs attributable to this hemisphere. The EEG, however, often shows abnormalities indicative of ischaemic disturbances on the opposite side and there are indications from cerebral angiography that there is a concomitant slowing of the contralateral circulation.

These findings are not only of theoretical interest but they appear to have practical importance for the differential diagnosis of cerebral lesions in older patients.— [Authors' summary.]

436. Head Injuries as a Factor in the Aetiology of Intracranial Meningioma

F. WALSHE. Lancet [Lancet] 2, 993-996, Nov. 4, 1961. 3 refs.

EPILEPSY

437. Neuro-physiology and Behaviour Disorders in Epileptic Children

E. J. A. NUFFIELD. Journal of Mental Science [J. ment. Sci.] 107, 438-458, May [received July], 1961. 4 figs., bibliography.

There is considerable controversy whether behaviour disorders occur in epilepsy post hoc or propter hoc. The relationship between different neurophysiological types of epilepsy and disturbances in behaviour has been investigated at the Maudsley Hospital, London, 322 children between the ages of 1 and 15 years seen between 1947 and 1956 being studied. They were classified into those with (a) rhinencephalic involvement, (b) centrencephalic involvement, (c) both, and (d) neither. The first two groups were those with temporal lobe foci (the "petit mal" group) with classic 3-c.p.s. spike-and-wave appearances in the electroencephalogram (EEG). The third group were those with irregular spike-and-wave or slow spike-and-wave discharges and the last group were those with verified non-temporal convexity foci.

In an attempt to demonstrate a qualitative and statistical basis for the behaviour differences in the 4 main EEG groups the behaviour disturbances chosen were aggression, neurosis, and anti-social behaviour. In this series of cases the gross incidence of behaviour disorders was high (59.6%) presumably owing to selection. The ratio of boys to girls was 5:3, with an even higher proportion of boys in the age groups 1 to 3 years (87.5%) and 4 to 6 years (71%). The I.Q. test was carried out in 288 cases, the mean being 89, which compared favourably with a control group of children not suffering from epilepsy, in whom the mean I.Q. was 91. The construction of behaviour ratings was possible owing to the routine use of Cameron's adaptation of Kanner's schema in taking the psychiatric history, the behavioural ratings being carried out without knowledge of the physiological group to which the child belonged.

Before correlating the EEG findings with the behavioural data all cases which fell into more than one EEG category were eliminated, as were those with doubtful cortical foci or foci that failed to appear consistently. Patients with an I.Q. of less than 50 and those below 3 years of age were also excluded, which left 233 cases. These were placed in 7 EEG groups: (1) temporal focus, (2) parietal or central, or occipital or frontal focus ("controls"), (3) 3-c.p.s. spike-and-wave, (4) irregular (and slow) spike-and-wave, (5) diffuse spikes, (6) non-specific abnormal, and (7) normal. Statistical analysis showed that the children with temporal lobe epilepsy were more aggressive than the "controls" those with 3-c.p.s. spike-and-wave more neurotic than the "controls", and those with irregular spike-and-wave intermediate between the other two. An attempt was made to correlate behaviour disorders with clinical groups, but the results failed to show as clear-cut a difference as with the electroencephalographic cate-David Morris

438. Yawning and Epilepsy

L. GOLDE and J. M. GREEN. Journal of Psychosomatic Research [J. psychosom. Res.] 5, 263-268, Oct., 1961. 11 refs.

A study of the association between yawning and spikeand-wave episodes in the electroencephalogram (EEG) in patients with petit mal epilepsy is reported in this paper from the Institute of Psychiatry, University of London, and the Maudsley Hospital, London. In 3 patients simultaneous recordings were made over a long period of the EEG, respiratory changes, the psychogalvanic reflex, and pulse changes. The experimental periods were divided up into periods of silence (lapse of conversation with the interviewer of more than 20 seconds), periods of conversation, spike-and-wave attacks, and a resting period during which the patient was left alone in the room. A comparison was made between the incidence of yawns or sighs associated with attacks and with a 20-second period preceding the onset of spikeand-wave episodes, and the incidence during the rest of the time recorded. It was found that yawns and sighs occurred significantly more frequently during periods of stimulation than during periods of silence and inactivity. There was a significant relationship between yawning or sighing and the onset of spike-and-wave attacks on the one hand and between these and psychological stimula-J. B. Stanton tion on the other.

439. Effects of Drugs on Secondary Epileptogenic Lesions

F. Morrell and L. Baker. Neurology [Neurology (Minneap.)] 11, 651-664, Aug., 1961. 10 figs., bibliography.

The authors report from the University of Minnesota Medical School, Minneapolis, the results of animal experiments undertaken to investigate the development of secondary epileptogenic areas in focal epilepsy and the effect of anticonvulsant drugs upon these. In 50 guineapigs chronic local epileptic lesions were produced by the application of aluminium hydroxide gel and ethyl

chloride spray to the brain exposed through a burr hole. In half the animals these lesions were made over the motor cortex and in the other half over the visual cortex. Primary epileptogenic lesions developed in all but 2 of the animals. They were then divided into 3 treatment groups and given respectively 20 mg. of phenobarbitone daily, 40 mg. of diphenylhydantoin daily, and 10 mg. of chlorpromazine daily; the remaining, untreated, animals formed a control group. In the treatment groups the electroencephalogram (EEG) was recorded after one month, when the drugs were then stopped abruptly and the EEG again recorded 4 to 7 days later. In 10 of the control animals EEGs were taken after one month and they were then given phenobarbitone for 4 weeks, at the end of which further EEG recordings were obtained and repeated after abrupt cessation of the drug. In the remaining control animals EEGs were recorded two months after operation. In this way the evolution of primary and secondary (mirror) epileptic foci could be observed.

It was found that only phenobarbitone retarded the development of the secondary epileptic foci, although diphenylhydantoin could abolish the clinical manifestations of the epilepsy. This difference in the action of these two anticonvulsant drugs is discussed in the light of their pharmacological properties and it is suggested that the development of secondary epileptic lesions is based on a synaptic bombardment of the neurones in the "mirror" region through commissural pathways rather than on an ephaptic recruitment of surrounding cells into the epileptiform discharge. The authors point the possible moral for the clinical neurologist of the differing effects of phenobarbitone and diphenylhydantoin in suppressing the development of secondary epileptic foci · in these animals. J. B. Stanton

440. Dilantin Toxicity: a Clinical and Electroencephalographic Study

E. ROSEMAN. Neurology [Neurology (Minneap.)] 11, 912-921, Oct., 1961. 5 figs., 3 refs.

In a series of over 3,000 cases of epilepsy diphenylhydantoin sodium was given alone or in combination with other anticonvulsant drugs. The author of this paper from the University of Louisville School of Medicine, Kentucky, considers that the only limitations to the use of this drug are: (1) it may elicit minor seizures. including classic petit mal, myoclonic, and akinetic fits and (2) its toxicity. The most common toxic effect is mild or severe "inebriety" resembling the picture seen in cerebellar disease; this occurred in over 45% of the last 1,000 cases treated. The electroencephalogram is affected by diphenylhydantoin only when the dosage approaches the toxic range. In fact, the combination of the appearance of mild toxic symptoms and slowing of the alpha rhythm can be used as a "satisfactory index to judge the titrating end-point of a particular dosage" in. the effective management of patients with epilepsy. In all cases of inebriety due to diphenylhydantoin the picture is reversible. Toxic effects of the drug which are not related to the dosage include gingival hypertrophy, gastro-intestinal disturbances, skin rashes, hirsutism,

and blood dyscrasias. Most of these are innocuous, and with the exception of the blood dyscrasias and possibly skin rash are not indications for cessation of treatment.

A. G. Freeman

PERIPHERAL NERVES

441. Sensory Nerve Conduction in Patients with Diabetes Mellitus and Controls

A. W. DOWNIE and D. J. NEWELL. Neurology [Neurology (Minneap.)] 11, 876-882, Oct., 1961. 6 figs., 6 refs.

Conduction rates in the sensory fibres of the median and ulnar nerves were measured in a group of 39 diabetic patients, 23 of whom had clinical evidence of peripheral neuropathy, and in 41 controls. A relatively simple method of detecting impairment in sensory nerve function is described. The conduction rates were significantly slower in diabetic patients with peripheral neuropathy than in diabetics without neuropathy, and these rates, in turn, were slower than those in normal controls. In all three groups conduction rates slowed progressively over the age of 35. The authors consider that measurement of conduction rates in sensory fibres should provide an objective method of following the course of diabetic neuropathy and its response to treatment.

A. G. Freeman

442. The Brachial Neuropathies

W. A. LISHMAN and W. R. RUSSELL. Lancet [Lancet] 2, 941-947, Oct. 28, 1961. Bibliography.

The history of the various theories propounded over the past half-century to account for pain in the arm are summarized. Many of these have always seemed bizarre to most neurologists. At the United Oxford Hospitals a group of 146 patients has been studied who all had the common feature of pain in the arm. This was attributed (largely retrospectively) in 78 cases to the carpal tunnel syndrome, in 50 to irritation of the cervical roots, in 3 to compression at the thoracic outlet, and in 3 to "frozen shoulder". In 12 cases no particular cause was found. The authors discuss the treatment of these patients and propound the [remarkable] theory that some patients suffering from compression of the median nerve in the carpal tunnel may be relieved by wearing a collar. They go farther and suggest that in time the surgical treatment of carpal tunnel compression is likely to disappear. It is suggested that there is considerable overlap of the multiple causes of pain in the arm and that root pain from a disk prolapse and compression in the carpal tunnel not infrequently coexist.

[Few neurologists would agree with the general views expressed in this paper. The following sentences are unintelligible—"This is not to suggest that 'pure' examples of nerve-root, thoracic-inlet or carpal-tunnel compression do exist. There is very strong evidence that they do; but in our cases there seemed to be much overlap." It would seem that an important "not" has been omitted. The reference to Garland (1957) is incorrect and should read Garland, Bradshaw and Clark.]

Hugh Garland .

Psychiatry

443. Apparently Non-indolic Ehrlich-positive Substances Related to Mental Illnesses

D. G. IRVINE. Journal of Neuropsychiatry [J. Neuropsychiat.] 2, 292-305, Aug., 1961. 19 refs.

Many authors have described a relationship between certain mental illnesses and the excretion of various indole compounds in the patient's urine. These studies were usually based on paper chromatography, utilizing an isopropanol-ammonia solvent followed by colour development with Ehrlich's reagent. In the present study, carried out at Saskatchewan Hospital, Canada, over a period of 2 years, emphasis has been placed on the highest Rf compounds rather than on the low Rf indolic carboxylic acids and indoxyl and skatoxyl sulphates investigated in most previous studies. The methods employed are described and the design of the study is discussed at great length; the results were statistically evaluated by means of the chi-square test and converted into the corresponding "probability" (P) values.

They showed that the metabolites studied could be

They showed that the metabolites studied could be divided into two groups. One was associated with psychoses in general (P=0.057) and a similar substance was significantly related to depression (P=0.019). It is suggested that these compounds may be more closely related to pyrroles than to indoles. The author emphasizes that the results represent associations only, and that no judgment about the actiological significance of the findings can yet be made.

B. M. Davleš

444. A Card Sorting Test Helpful in Making Psychiatric Diagnosis

A. HOFFER and H. OSMOND. Journal of Neuropsychiatry [J. Neuropsychiat.] 2, 306-330, Aug., 1961. 2 figs., 20 refs.

This paper from Saskatchewan University Hospital, Saskatoon, describes the development and use of a cardsorting test designed to separate patients with schizophrenia from those with other mental disorders and from normal subjects. The test, known as the Hoffer-Osmond diagnostic (HOD) test, can easily be administered by a lay person. It comprises 145 questions, each typed on a small white card, divided into groups designed to measure respectively visual, auditory, tactile, and olfactory perception as well as thought processes, feelings, and time perception. In giving the test the cards, well shuffled, are handed to the subject, who according to his answer places them in one of two boxes marked "true" or "false"; the method of scoring, which is described, is based on the number of cards in the "true" box. The results of applying the test to a number of normal subjects and patients with different psychiatric illnessés are presented and analysed. The authors claim that the test can successfully distinguish schizophrenia from all other mental illnesses except organic disease (toxic confusional states) with a high degree of probability. B. M. Davles

445. A Chromatographic Study of the Amino Acids in Urine and C.S.F. from Mentally Deficient Children E. McKay and H. Thom. Journal of Mental Science

E. MCKAY and H. IHOM. Journal of Mental Science [J. ment. Sci.] 107, 261-267, March [received Aug.], 1961. 11 refs.

At the Royal Hospital for Sick Children, Aberdeen, the amino-acids present in the urine and cerebrospinal fluid (C.S.F.) of 32 known idiots or imbeciles and 8 children with apparently gross mental subnormality were investigated by means of paper chromatography. The patients ages ranged from 18 months to 21 years, and 25 were males and 15 females. In the one random sample of urine examined in each case no protein, glucose, sucrose, cystine, or phenylpyruvic acid was present. Glycine and alanine were found in all chromatograms. Histidine, serine, glutamine, threonine, ethanolamine, glutamic acid (break-down from glutamine), tyrosine, leucine, valine, taurine, histamine, aspartic acid, lysine. arginine, and β -amino isobutyric acid were present in that order in from 95 to 13% of the chromatograms. The spot intensities were greatest for glycine, alanine, histidine, serine, and glutamine. In the C.S.F. the number of cells, total protein and globulin levels, and the Wassermann reaction were normal. Glutamic acid and glutamine were present in all chromatograms, while alanine, glycine, leucine, threonine, valine, serine, tyrosine, aspartic acid; histidine, arginine, and lysine were present in from 93 to 5% of the chromatograms; here the intensities were greatest for glutamic acid and glutamine.

Comparison with these results with those for normal children as reported in the literature showed that glutamine, glutamic acid, alanine, glycine, leucine, valine, and threonine were prominent in both groups. However, aspartic acid, serine, tyrosine, and lysine were found much more frequently in normal children, but histidine was not found at all by Logothetis (17 specimens) although in 54% of 26 cases by Walker. A moderate correlation between urinary and C.S.F. findings was noted in specimens with a high amino-acid content. An attempt to establish some relationship between these findings and the clinical condition was unsuccessful, specific clinical traits being uncommon in these cases of primary oligophrenia.

[Particulars of the method of collection of specimens of C.S.F. are not given.]

G. de M. Rudolf

446. A Clinical and Biochemical Study of Monoamine Oxidase Inhibition in Depressed Patients. I. A Clinical Trial of Nialamide

W. G. DEWHURST and C. M. B. PARE. Journal of Mental Science [J. ment. Sci.] 107, 239-243, March [received Aug.], 1961. 5 refs.

In this, the first of two papers [see Abstract 447] from the Bethlem Royal and Maudsley Hospitals, London, the authors describe a controlled double-blind trial of N-Isonicotinoyl (N-N-benzylcarboxamidoethyl)

hydrazine (nialamide) in 28 depressed patients, who were rated clinically each week throughout the trial. All the patients were initially given the active drug in a dosage of 25 mg. 3 times a day for 2 weeks followed by 50 mg. 3 times a day for a further 2 weeks. Thereafter, unknown to patient, doctors, or nurses a placebo was substituted; as the active drug was free from side-effects this procedure was possible.

Of the 28 patients, 7 improved and in 4 of these the improvement could be attributed to the action of the drug. No clinical toxic effects were noted. It is emphasized that, in contrast to electric convulsion therapy, nialamide did not cure the depression but afforded symptomatic relief as long as administration continued or until a natural remission occurred. B. M. Davies

447. A Clinical and Biochemical Study of Monoamine Oxidase Inhibition in Depressed Patients. II. 5-Hydroxy-tryptamine Tolerance before and after Nialamide

W. G. DEWHURST and C. M. B. PARE. Journal of Mental Science [J. ment. Sci.] 107, 244-249, March [received Aug.], 1961. 2 figs., 6 refs.

In the second paper [see Abstract 446] a study is reported of the action of the monoamine oxidase inhibitor nialamide in the treatment of 18 of the depressed patients described above. Before and after administration of the drug a 5-hydroxytryptamine (5-HT) tolerance test was performed. While the part played by 5-HT in depression is not clear, the monoamine oxidase inhibitor can be tested by giving 5-HT as the substrate with the drug to be tested and assaying the major metabolite, 5-hydroxyindole acetic acid, in the urine.

It was found that nialamide inhibited monoamine oxidase activity in these depressed patients. Moreover, none of the patients showed any clinical improvement in their depression which could be correlated with the level of monoamine oxidase inhibition. In one patient who responded well to the drug there was no evidence of monoamine oxidase inhibition.

The validity of the 5-HT tolerance test as an indicator of cerebral monoamine oxidase activity is discussed.

B. M. Davies

448. Fibrosis of the Pia Mater in Schizophrenia. (Фиброз мягких мозговых оболочек при шивофрении)

P. B. KAZAKOVA. Журнал Невропатоловии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1244—1250, No. 8, 1961. 3 figs., 21 refs.

This paper from the Research Institute of Psychiatry, Moscow, reports the naked-eye appearances of the brain and meninges at the time of operation for prefrontal leucotomy and the results of the microscopical examination of biopsy material in 30 cases of undoubted, uncomplicated schizophrenia. The patients ranged in age from 21 to 52 years and the duration of their illness from one to 22 years.

At operation there was cystic dilatation of the subarachnoid space and here the cerebrospinal fluid had sometimes acquired a gelatinous consistency. The vessels of the subarachnoid space (mainly veins) showed stasis and engorgement. The pia mater of the surface of the hemisphere showed marked oedema, opacity, and fibrosis.

The biopsy material was stained for argyrophil and elastic fibres by Nissl's and van Gieson's methods and with haematoxylin and eosin. There was distortion of the nerve cells of the outer layers of the cortex and swelling and destruction of the nerve cells of the inner layers, at times of a focal character. These changes were especially marked in the frontal lobes. The astrocytes showed amoeboid forms and pyknosis. The microglia was atrophic, but the oligodendroglia was dense and proliferating. In 20 cases, in most of which, regardless of age, the duration of illness was 6 years or more, the subarachnoid trabecular tissue was coarse, collagenized, and sometimes completely fused with the grey matter. Here there was massive, tumour-like formation of the collagen fibres in the form of coarse, thick bundles often nearly obliterating the subarachnoid space. In the depth of the sulci the trabeculae remained fine and the trabecular spaces were dilated with oedema fluid. There were no inflammatory changes in the pia mater. In the remaining 10 cases there was no fibrosis in the subarachnoid space, but significant coarsening and collagenization of the argyrophil components of the pia mater and arachnoid mater. The large pial veins showed perivenous fibrosis. The author considers schizophrenia to be a toxic-hypoxic encephalitis of which these pathological changes are the end result.

[The author does not state what treatment the patients had had previously.] $G. P. McG\'{o}vern$

449. Schizophrenia and the Family: a Survey of the Literature 1956–1960 on the Etiology of Schizophrenia. [In English]

J. FOUDRAINE. Acta psychotherapeutica et psychosomatica [Acta psychother. (Basel)] 9, 82-110, 1961. Bibliography.

TREATMENT

450. Taractan (Chlorprothixene) as a Neuroleptic Drug in Clinical Psychiatry

H. GROSS and E. KALTENBAECK. Diseases of the Nervous System [Dis. nerv. Syst.] 22, 502-507, Sept., 1961.

Drugs suitable for sedation in cases of agitation are designated basal neuroleptics and, ideally, should have the following qualities: (1) prompt and reliable action; (2) no painful reaction at the injection site; (3) minimal motor and psychic side-effects; (4) no vasomotor reactions; and (5) absence of other side-effects and allergic reactions in the nursing attendants. The authors, at Steinhof Hospital, Vienna, have treated 426 male patients with a new neuroleptic, "taractan" (chlorprothixene), which is similar to chlorpromazine. They were favourably impressed by the drug, which has a potentiating effect on other narcotics and is effective in small doses by mouth. The present report, however, is concerned only with the 312 patients who were given taractan parenterally as a basal neuroleptic. Given in this way the drug

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was found to be principally suitable for initial sedation in agitation, and the authors did not observe the antidepressive effect described by others, as the soporific action was strong. It was most effective in cases of affective reaction and less so in schizophrenia. The five requirements for a neuroleptic mentioned above were quite well fulfilled. Side-effects included an almost invariable tachycardia, pallor, and drying of the mouth, which did not seem serious disadvantages. There were a few instances of hyperthermia, the tongue-pharynx syndrome, trismus, and ocular spasm.

An initial dose of 30 mg. was given, followed if necessary by a further dose of 30 to 60 mg. within the first hour. The same dose was repeated twice within 24 hours to a total of 90 to 180 mg. and thereafter at 8-hourly intervals. In a few catatonic or manic cases a daily dose of 270 to 460 mg. was necessary. Within 3 days in most cases sedation was complete and the injection route could be discontinued, oral treatment being substituted. Basic drive was much reduced, and resistance to taking nourishment and tablets by mouth overcome.

Taractan potentiates alcohol and is not suitable for acute alcoholic intoxication. The authors also had poor results in arteriosclerotic confusion. The chief role of taractan is as a safe neuroleptic in agitation, as a prelude to longer treatment with other drugs.

Gavin Thurston

451. Chlorprothixene: a New Psychotropic Entity J. RAVN. American Journal of Psychiatry [Amer. J. Psychiat.] 118, 227–231, Sept., 1961. 1 fig., 4 refs.

This paper from Middlefart Mental Hospital, Denmark, reports an uncontrolled trial of chlorprothixene. one of the thiaxanthene group of compounds in which the nitrogen atom in the phenothiazine ring has been replaced by an unsaturated carbon atom. This modification is regarded as important, since it is this part of the phenothiazine molecule which is suspected of producing the well-known toxic effects of the phenothiazines. The author has used chlorprothixene in the treatment of 600 patients during a period of 18 months in preference to all other psychotropic drugs. The present report is concerned with 338 male patients who received the drug for 3 months or more, doses of up to 80 mg. 3 times a day being given intramuscularly to agitated patients. A satisfactory response was usually obtained from a daily dose of 400 to 500 mg. given orally in divided doses.

Moderate improvement was noted in 70% of patients diagnosed as suffering from paranoid schizophrenia. However, patients with other types of schizophrenia did not do so well and only one out of 83 schizophrenics showed "marked" improvement. Affective disorders were noted to respond very much better, a "marked or moderate" improvement being claimed for 80%. [The criteria for improvement and comparative data for untreated or otherwise treated groups are not given.]

Among the first 100 patients on whom blood counts, were performed on alternate days, only one showed mild leucopenia, which cleared up when the drug was withdrawn; there was no change in the neutrophil or granulo-

cyte count in any of the cases. Urine analysis and tests of liver function gave normal results in all patients throughout treatment, and no changes were noted in the daily blood pressure. In the entire series of 600 patients treated, some with doses of up to 800 mg. daily, no extrapyramidal signs have been noted. Dryness of the mouth has been noted in one-fifth. Lassitude occurred in about one-third of the patients but is not as prominent a feature as with the phenothiazine drugs. No other serious side-effects were noted. A few cases in which the drug has been used successfully in the withdrawal treatment of patients addicted to alcohol, barbiturates, or morphine are also reported. The danger of potentiating phenothiazine derivatives is noted. It is concluded that chlorprothixene is an "effective broadrange psychotropic agent with a high degree of safety". Christopher Wardle

452. Clinical Evaluation of Fluphenazine in the Treatment of Psychotic Patients

J. P. HOLT and E. R. WRIGHT. Diseases of the Nervous System [Dis. nerv. Syst.] 22, 513-519, Sept., 1961. 11 refs.

Failure of drugs to effect any improvement in chronic psychoses has a bad effect on the morale of both patients and staff in chronic mental wards. However, the improvement, even of a few patients, with new drugs may materially alter this picture so that a constant search for more effective remedies is justified. The present paper reports a clinical trial of a new phenothiazine derivative, fluphenazine ("prolixin") on 50 patients at Embreeville State Hospital, Pennsylvania. The patients were all long-term cases, the average stay in hospital having been 4.8 years. They included schizophrenics, manic-depressives, and organic reaction types. They all caused much trouble in management. Various ataractics, electric convulsion therapy, and other treatment had been used previously without improvement. The dosage of fluphenazine varied widely, the initial dose ranging from 1 to 22.5 mg, daily and the maintenance dose from 1 to 15 mg. daily. Assessment was made by observation and interviews by physicians and other staff. Treatment was continued for at least 70 days before the final evaluation was made.

Seven patients (14%) were markedly improved, 22 (44%) moderately improved, and 21 (42%) unchanged. Reduction in agitation and tension was the most striking effect in the successful cases and produced better social integration, with reduction in aggression and improved cooperation. Deluded and hallucinatory behaviour also benefited. Side-effects were similar to those of other phenothiazine drugs, including drowsiness; dry mouth, and lethargy. There were a few dyskinetic reactions, with dysphagia, torticollis, and ocular spasms. Parkinsonism developed in 4 cases. Hypotension was not recorded.

Fluphenazine is a powerful agent with rapid onset of action and has a more prolonged effect than any other ataractic in the authors' experience. The margin between effective dosage and troublesome side-effects is small. Extrapyramidal reactions, though annoying, did not hinder progress.

Gavin Thurston

Dermatology

- 453. Contribution to the Study of the Soluble Proteins of the Human Skin by Means of Electrophoresis and of Immuno-electrophoresis in Agar Medium. (Contribution à l'étude des protéines solubles du derme humain à l'aide de l'électrophorèse et de l'immuno-électrophorèse en milieu gélifié)
- J. ZIMMER, F. WORINGER, and M. T. Dub. Annales de dermatologie et de syphiligraphie [Ann. Derm. Syph. (Parls)] 88, 376–384, July-Aug., 1961. 3 figs.

While the mucopolysaccharides of the skin are relatively well know, few facts have been published about the soluble proteins, and these have therefore been investigated by the authors at the Dermatological Clinic of the Faculty of Medicine, Strasbourg. Normal human skin was frozen immediately after excision with liquid nitrogen and the proteins then fixed in a 2% acetic acid solution after electrophoresis.

The electrophoretic pattern showed the presence of soluble proteins in the skin. Whereas the bands made by serum albumin are longest transversely, those made by skin albumin were elongated in the direction of the electrophoretic strip. No α_2 globulins could be found in the skin. The bands corresponding to the β globulins resembled those found in serum, but were much wider. No difference was found between the γ globulins of the serum and those of the skin. Immuno-electrophoresis in an agar medium was then performed in order to discover, from the antigenic aspect, the relationship between dermal proteins and serum proteins and to confirm and define the differences already revealed by simple electrophoresis. By this means it was shown that the serum proteins and dermal proteins are antigenically identical. Certain substances present in serum were found, however, to be absent from skin, namely, seromucoidic acid, 3 to 4 α_2 globulins, and β_1 C-globulin. One of the β_2 globulins was clearly present in skin, whereas only a trace could be found in serum. From these results it is suggested that anabolic reactions with protein as well as with mucopolysaccharides occur in the skin.

E. Lipman Cohen

454. Tolbutamide in the Treatment of Skin Diseases I. Singh, M. L. Gaind, and D. Jayram. British Journal of Dermatology [Brit. J. Derm.] 73, 362-366, Oct., 1961. 12 refs.

Having observed that patients given tolbutamide keep a remarkably clear scalp and are practically free from skin complications, the authors tried this drug in the treatment of various skin conditions. In most cases of seborrhoeic eruptions and dandruff the response was good, although dandruff tended to recur when the drug was withdrawn. Some cases of acne vulgaris and psoriasis, particularly flexural psoriasis, responded well, and in 3 out of 4 cases of dermatitis herpetiformis there was complete clearing. On the basis of 7 cases of vitiligo

treated it is stated that the progress of the condition was halted and there was "an attempt at repigmentation". All 9 patients with pityriasis alba were cured. The dosage of tolbutamide was 0.5 g. to 1.5 g. daily. It was well tolerated and there were no allergic skin reactions. None of the patients suffered from frank or latent diabetes mellitus. Significant lowering of the blood sugar level was recorded in only one case during tolbutamide therapy.

E. W. Prosser Thomas

455. Clinical Evaluation of Fluorandrenolone, a New Steroid, in Dermatological Practice

A. ROSTENBERG JR. Journal of New Drugs [J. new Drugs] 1, 118-121, May-June [received Sept.], 1961. 1 ref.

Fluorandrenolone (6α -fluoro- 16α -hydroxyhydrocortisone 16:17-acetonide) is a new synthetic steroid which has been found to have powerful anti-inflammatory action. In the present study, reported from the University of Illinois College of Medicine, Chicago, it was used in a concentration of 0.05% in a cream base with and without neomycin and in an ointment base. [No distinction is drawn between these 3 formulations in reporting the results of treatment.]

A series of 144 patients, mostly ambulatory, of both sexes and displaying a wide variety of dermatological conditions were treated. They were supplied with a fluorandrenolone preparation and examined weekly. The effect of treatment was assessed after 3 weeks if the condition had not responded sooner. For ease of assessment the patients were divided into eczematous and non-eczematous groups. The results were particularly good in the eczematous group, in which 76% showed a "good" or "excellent" response, only 8 of 108 cases being unimproved. The results were not so striking in the non-eczematous cases, but the anti-inflammatory effect was apparent in these also.

A fourfold increase in concentration of the steroid did not significantly improve the results. No allergic sensitization was noted. Serum and urine tests on 5 patients who were using 1 to 3 tubes containing 15 g. of fluorandrenolone daily for 3 to 20 days, showed no evidence of absorption of the steroid. E. H. Johnson

456. Evaluation of Flurandrenolone: a New Topical Corticosterold

H. R. GRAY, R. L. WOLF, and R. H. DONEFF. Archives of Dermatology [Arch. Derm.] 84, 18-21, July, 1961. 9 refs.

For the purpose of studying the anti-inflammatory effect of flurandrenolone, a new synthetic steroid with the formula 6α -fluoro- 16α -hydroxyhydrocortisone 16:17-acetonide, an experiment on 25 healthy male volunteers was carried out at Marion County General Hospital, Indianapolis. Standardized and comparative patch tests were applied, using tetrahydrofurfuryl alcohol

(THFA), a primary irritant, alone and in combination with 1% hydrocortisone acetate and 0.05% flurandrenolone. The results, examined independently by 2 observers, were closely correlated and showed the production of considerably less erythema in 23 of the 25 cases after the application of flurandrenolone with THFA as compared with that after THFA alone. THFA with flurandrenolone also produced less erythema than THFA with hydrocortisone, but the difference was not so great, although considered statistically significant.

In a clinical study at the same hospital 160 patients with a variety of dermatoses, mainly of types which usually show a good response to topical corticosteroids, were treated with a 0.05% flurandrenolone cream or ointment. No side-effects were noted during a follow-up of 1 to 18 weeks. "Good" or "excellent" results were obtained in 79% of the cases and partial improvement in a further 18%.

The authors found flurandrenolone to be a safe and effective topical corticosteroid which merits further study.

Benjamin Schwartz

457. Treatment of Localized Neurodermatitis and Prurigo Nodularis by Intradermal Injections of Methylene Blue in Procaine. (Лечение ограниченного невродермата и увловатой почесухи внутрикомными инъекциями раствора метиленовой сини в новокаине) М. М. Žецтакоv, Ju. К. Skripkin, and L. D. Tiščenko. Вестник Дерматологии и Венерологии [Vestn. Derm. Vener.] 35, 33–37, July, 1961. 1 fig., 13 refs.

The authors describe the treatment of neurodermatitis and nodular prurigo by the intradermal injection of a 0.5 to 1% solution of methylene blue in 2% procaine. The solution must be injected intradermally as sterile abscesses may form if it is injected subcutaneously. A photograph of a needle devised to ensure intradermal injection is reproduced.

Anogenital pruritus and other types of focal neurodermatitis, circumscribed focal eczema, and nodular prurigo were treated. The injections were given once every 3 days and courses of 5 to 9 injections were required. Out of the 48 patients treated, 22 were cured, 14 improved, and 12 were not affected. This method is not suitable for eczema in its acute stages. Natalie Hopewell

458. Physiology and Pharmacology of the Skin 1959/60. [Review Article, in English]

G. H. FINDLAY and R. KOOU. Dermatologica [Dermatologica (Basel)] 123, 57-86, July, 1961. Bibliography.

459. Light Sensitivity Treated by Hyposensitization K. J. JOHNSON. Annals of Allergy [Ann. Allergy] 19, 891–893, Aug. [received Oct.], 1961. 11 refs.

The author reports a case of sensitivity to light, seen in private practice in North Dakota, in which a female schoolteacher (a nun) aged 45 developed redness and small vesicles on the exposed parts of the hands and face, sometimes with oedema, during the summer, particularly when outdoors or exposed to the sun. No L.E. cells were found in blood smears, no porphobilinogen could be identified in the urine, and the patient had not taken

any drug likely to cause photosensitivity for several years previously. Treatment with corticosteroids had an excellent therapeutic effect, but the trouble recurred on their withdrawal. Ultraviolet irradiation was therefore tried, beginning with an exposure of 3 seconds, and very gradually increasing the exposure period each day. When an exposure of 40 seconds was reached the patient could move out of doors without recurrence of sensitivity, but ultraviolet irradiation has had to be repeated every 2 weeks.

H. Herxheimer

460. Herpes Zoster and Malignancy

E. T. WRIGHT and L. H. WINTER. Archives of Dermatology [Arch. Derm.] 84, 242-244, Aug., 1961. 6 refs.

After a brief review of the literature on the association between herpes zoster and neoplastic disease the authors report the results of their own investigation on 55,279 male patients admitted to the Veterans Administration Center Hospital, Los Angeles, during the years 1954 to 1958 inclusive. Of these patients 147 (0.26%) had herpes. zoster, 113 (0.22%) of the cases occurring among the 51,202 patients with non-neoplastic disease and 34 (0.85%) among the 3,987 patients with malignancy. Thus the incidence of herpes zoster was approximately four times greater in the neoplastic than in the nonneoplastic cases. A table giving data regarding the types and sites of malignancy concerned shows that of 3,449 patients with various types of carcinoma 16 (0.46%) had herpes zoster, whereas of 538 with some type of lymphoma, zoster occurred in 18 (3.34%). Except for those with chronic lymphatic leukaemia, most patients developed the herpes zoster after the onset of malignancy. Histologically there was no difference between the herpetic lesions in the malignant and non-malignant cases, but sections of the skin lesions from patients in the lymphoma group showed somewhat deeper, more destructive, and necrotic changes extending into the dermis'.

Commenting on their findings the authors are unable to suggest a reason for the apparent increase in the frequency of herpes zoster in patients with neoplastic diseases other than lymphoma; the association with the latter has been previously reported and is confirmed by this study. Although the number of their cases was too small to be statistically significant, they consider that the development of herpes zoster in patients with Hodgkin's disease or pulmonary malignancy is an unfavourable prognostic sign.

Benjamin Schwartz

461: Acrodermatitis Enteropathica. (К вопросу об acrodermatitis enteropathica)

A. V. HAMAGANOVA and A. A. ANDROSOVA. *Becmhuk Дерматоловии и Венероловии [Vestn. Derm. Vener.*] 35, 67-71, Aug., 1961. 3 figs., 2 refs.

The authors describe 3 cases of the condition known as acrodermatitis enteropathica, which was first described in 1942 by Danbolt and Closs (Acta derm.-venereol. (Stockh.), 36, 257). This condition is very rare and presents a diagnostic problem, since it is easily confused with epidermolysis bullosa, dermatitis herpetiformis, pustular psoriasis, and acrodermatitis. It occurs mostly in children, and presents as a vesiculo-bullous eruption affecting

the hips, buttocks, external genitalia, groins, elbows, the mouth region, and the ears and nose. There is a total alopecia, with photophobia and usually also intestinal disturbance.

Two of the present patients were initially treated with prednisolone and vitamins, but without benefit. They were then treated with iodochloroxyquinoline, which produced marked improvement, although it is too early yet to regard it as curative. The authors quote another case described in Austria in which this drug produced only little improvement. They consider that the treatment of this condition merits further study.

N. Hopewell

462. Treatment of Plantar Warts in Children C. F. H. VICKERS. British Medical Journal [Brit. med

C. F. H. VICKERS. British Medical Journal [Brit. med. J.] 2, 743-745, Sept. 16, 1961. 8 refs.

In view of the reported success in the treatment of plantar warts of soaking the foot in a solution of formalin the author undertook both a retrospective survey of 465 children and a prospective survey of 200 consecutive patients given this treatment at the Sheffield Royal Infirmary. Of the retrospective series only 19 patients were untraced so that the final survey included 646 children. After scale and dead tissue had been removed from the top of the wart by scraping with a nail-file-or the side of the blade of a pair of scissors the wartbearing part of the foot was immersed for 15 to 20 minutes in a 3% solution of formalin, the process being repeated each night. If necessary, the strength of the formalin solution was increased after 3 weeks, even upto 10%. To prevent interdigital cracks petroleum jelly was applied before starting treatment.

It was found that 80% of all plantar warts up to 1 cm. in diameter were cured in 6 to 8 weeks. The author states that larger warts should be curetted after 3 weeks' treatment with formalin. Recurrences and reinfection rates were extremely low. Other advantages of the method are that it is simple to carry out and painless. On the other hand, it is time consuming and success depends upon "the cooperation of the patient and the enthusiasm of the doctor".

E. H. Johnson

463. Antibiotics and Pustulocystic Acne: a Long-term, Double-blind Evaluation

B. A. WANSKER. Archives of Dermatology [Arch. Derm.] 84, 96-98, July, 1961. 11 refs.

The subjects of this study were private patients, mostly female between the ages of 12 and 36 years, with pustulocystic acne. Using a double-blind method of comparison, the author studied the effects of various antibiotics on 91 patients who participated in the trial for at least 6 months. All patients used a resorcin and sulphur preparation at night and received local acne surgery consisting of incision and drainage of abscesses and cysts.

From the tabulated results it is seen that 74 patients received one or other of the broad-spectrum antibiotics erythromycin stearate and propionate, tetracycline phosphate and citric acid, triacetyloleandomycin, and tetracycline-novobiocin [3 doses daily; exact dosage not stated] and 17 received only a placebo. Of the antibiotic

group, 54 (74.3%) were reported as significantly improved and 20 (25.7%) as showing no essential difference when compared with the control group. The results of local treatment only in 5 (29.4%) of the control group were reported as being as good as those in the antibiotic group, but less improvement was noted in 12 (70.6%). There seemed to be no significant difference in the effectiveness of the several antibiotics used and no side-effects of any kind were noted, even when patients had taken antibiotics continuously for as long as 18 months. Benjamin Schwartz

464. The Treatment of Acne Vulgaris with Dapsone C. M. Ross. British Journal of Dermatology [Brit. J. Derm.] 73, 367-370, Oct., 1961.

A double-blind trial of dapsone in the treatment of acne vulgaris showed that the drug was beneficial in a significant percentage of cases. It is recommended as a cheap and safe alternative to the broad-spectrum antibiotics, although the latter drugs are more effective. The author emphasizes that dapsone should be administered with care; a dosage of 200 mg. daily should never be exceeded, the initial dosage being 50 mg. daily. The chief side-effects are headache and cyanosis due to methaemoglobinaemia.

E. W. Prosser Thomas

465. Personality of Students with Acne Vulgaris C. J. Lucas. British Medical Journal [Brit. med. J.] 2, 354-356, Aug. 5, 1961. 15 refs.

This paper from the Student Health Service, University College, London, compares the personalities of three groups of students: (1) controls with no acne; (2) students with acne who did not complain of it; and (3) students with acne who sought treatment for it. The Maudsley Personality Inventory (M.P.I.) was used to assess personality, this giving measures of "neuroticism" and "extraversion". Results were analysed at the end of the academic year, when the case record of each student was also examined to see whether there had been any attendances during the year with complaints of definite psychological symptoms.

Of the 44 students who took part in the study, 15 were controls, 12 had acne but made no complaint of it, and 17 had acne and sought treatment for it. The groups were of comparable age and sex distribution. There were no statistically significant differences between the mean scores of the three groups on either neuroticism or extraversion.

As an independent assessment the numbers attending with psychological symptoms during the year was determined; there were 5 in the control group, 2 in Group 2, and 5 in Group 3. Thus the acne groups scored no higher on a measure of neuroticism than did the control group, nor were they more prone to report psychological symptoms. When the presence or absence of reported psychological symptoms was related to M.P.I. scores it was found that the group reporting such symptoms had a significantly higher mean N score but not E score. This suggests that the negative findings when comparing acne and control groups is unlikely to be due to the invalidity of the test.

F. E. Kenyon

Paediatrics

466. Petechiae in the Newborn Infant

J. R. POLEY and G. B. STICKLER. American Journal of Diseases of Children [Amer. J. Dis. Child.] 102, 365-368, Sept., 1961. 5 figs., 5 refs.

The authors discuss petechiae in the newborn infant on the basis, initially, of their observation at the Mayo Clinic of 4 newborn infants in whom there was disseminated petechial bleeding of the scalp, face, and neck, associated with localized cyanosis and some oedema. All these infants had had at the time of delivery two or more loops of umbilical cord wrapped tightly around the neck, and further investigation led to the conclusion that local or regional increase in venous pressure during delivery may be an important factor in the causation of this condition.

To confirm this a study was therefore made of 250 newborn infants, 123 female and 127 male, who were examined between half an hour and 24 hours after delivery. This revealed that 44% of the infants had petechiae but these were of a more localized character than in the 4 initial cases. The petechiae showed a higher incidence in larger infants and in males, and their distribution was usually limited to that part of the body presenting at delivery. From these findings the authors conclude that the condition is probably caused by compression of the jugular veins during passage through the birth canal and that the mechanism is similar to that seen in compression injuries of the chest or acute mediastinitis (the superior vena cava syndrome); the condition is also sometimes observed in children with whooping-cough. As capillary fragility decreases with increasing birth weight they consider it unlikely that changes in capillary fragility contribute greatly to the production of petechiae in the newborn. R. G. Meyer-

467. Foefal Haemoglobin in Haemolytic Disease of the Newborn

T. E. Oppe and I. D. Fraser. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 507-510, Oct., 1961. 5 figs., 10 refs.

At Southmead General Hospital, Bristol, samples of cord blood were obtained at birth from 37 infants delivered prematurely suffering from haemolytic disease due to the rhesus factor. Samples were taken for comparison from 29 infants of similar gestational age not affected by haemolytic disease. The total haemoglobin content and the concentrations of foetal haemoglobin (HbF) and adult haemoglobin (HbA) were determined in each group.

There was an increased proportion of HbA in the affected infants as compared with the normal infants, and this was related to the severity of the disease. There, was also a decrease in the concentration of HbF which was related to the total haemoglobin concentration and an increase in the concentration of HbA which was poorly

correlated with the total haemoglobin concentration. These abnormalities were present from the 35th week of gestation.

It is suggested that these are the results to be expected from haemolysis and increased erythropoiesis at a time when the biosynthesis of HbA is steadily increasing.

E. H. Johnson

468. Metabolic Aspects of Idiopathic Respiratory Distress (Hyaline Membrane Syndrome) in Newborn Infants D. A. NICOLOPOULOS and C. A. SMITH. *Pediatrics* [*Pediatrics*] 28, 206-222, Aug., 1961. 4 figs., 32 refs.

At the Boston Lying-in Hospital metabolic studies were carried out during the first 48 hours of life in premature infants with respiratory distress of the hyaline membrane type and in infants with respiratory distress born to diabetic mothers. There was a significant increase in the non-protein nitrogen and potassium levels in blood and plasma in both groups of infants compared with control groups of similar infants without respiratory distress. These levels were also raised in extremely premature infants who had no respiratory distress. The urinary excretion of sodium and creatinine confirmed the increased catabolism associated with stress due to difficult respiration. The shifts of body water which occur with this metabolic disturbance are considered to be the result rather than the cause of respiratory distress. No. conclusions could be drawn, but further studies of early feeding are being carried out directed towards measures to prevent consumption of body tissue.

Margaret D. Baber

469. The Staphylococcus and the Newborn Child V. D. Plueckhahn. British Medical Journal [Brit. med. J.] 2, 779-785, Sept. 23, 1961. 3 figs., 34 refs.

Staphylococcal infection in newborn infants and their mothers is a problem which over the past decade has caused considerable concern to all in charge of maternity units. The present author reviews experience at the Geelong and District Hospital, Victoria, Australia, since 1956, both in respect of the incidence of staphylococcal infection and the various measures adopted to limit and control such infection. The incidence of minor staphylococcal infection fell from 41% in 1956 to 4.7% in 1960. and the incidence of staphylococcal skin disease from 30.8% to 1.3% in the same period. The most important factors responsible for this improvement were: (1) a restriction placed on nursing procedures such as daily bathing, frequent eye-toilet, weighing at each feed which necessitated frequent handling of infants; (2) roomingin; and (3) the application of hexachlorophane emulsion to the skin. During the period under review the incidence of maternal breast abscess fell from 2.5% to 0.6%, and the mortality and morbidity rates among infants during the first 6 months of life were also reduced.

R. M. Todd

CLINICAL PAEDIATRICS

470. Hypernatraemic Dehydration in Infantile Gastro-enteritis

D. MACAULAY and M. I. BLACKHALL. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 543-550, Oct., 1961. 1 fig., 14 refs.

After first describing the clinical features and biochemical findings in 2 infants aged 3 months and 10 weeks respectively admitted to the Duchess of York Hospital for Babies, Manchester, suffering from hypernatraemic dehydration associated with gastro-enteritis, the authors then present a review of the records of 100 consecutive infants with diarrhoea seen at the hospital since July, 1957, and in whom the serum electrolyte levels were investigated; they point out that these represented rather less than 25% of all infants admitted with diarrhoea. Serum sodium levels of 150 mEq. per litre or above were taken to constitute hypernatraemia and this occurred in .30 of the 100 cases reviewed. Disorders of the central nervous system, convulsions, lethargy and coma, or hyperirritability occurred in 19 (63%) of these hypernatraemic infants compared with 22 (31%) of the 70 with normal or low serum sodium levels. The apparent , degree of dehydration, clinically, did not differ in the two groups, the main difference being that the severity of the accompanying anorexia, the duration of the diarrhoea. the increase in temperature, and the degree of tachypnoca were all more marked in the hypernatraemic group. The development of hyperosmolarity is a consequence of the greater loss of water than electrolytes in the loose stools. In a brief discussion of treatment it is noted that the dev hydration is often difficult to correct, partly because the severe anorexia " may make it impossible to get enough fluid into the child" and partly because of the loss of electrolytes, especially potassium, the infantile kidneys. become incapable of excreting a concentrated urine.

Winston Turner

471. Acute Cor Pulmonale in Children. (Le cœur pulmonaire aigu infantile)

G. DECHAMPS. Acta cardiologica [Acta cardiol. (Brux.)] 16, 361-378, 1961. 4 figs., bibliography.

Although acute cor pulmonale is a relatively rare occurrence in paediatric practice, the importance of its recognition is emphasized in this report from the War Memorial Paediatric Clinic, Brussels. Among 125 children admitted with acute severe pulmonary disease, cor pul-- monale occurred in 17 (13%), of whom 9 were under 3 months of age. When it occurs it is of rapid onset and if suspected from the presence of peripheral circulatory failure, cardiac failure with hepatomegaly, and a tachycardia of 180 to 200 per minute then an electrocardiogram may confirm the diagnosis by showing inverted T waves in the right precordial leads, particularly V4R and V2, and a shift to the left of the transitional precordial complexes. The complication occurs early in the disease and carries a grave prognosis. The 6 deaths in the author's series occurred between the 4th and 16th days of the illness and bore no relation to the type of pulmonary lesion present. Once suspected and diagnosed rapid treatment with digitalis and noradrenaline is imperative.

[A good review of the relevant literature is to be found in the discussion, which is given more space than the clinical report.]

David Morris

472. A Haemolytic-Uraemic Syndrome in Infancy J. Griffiths and K. G. Irving. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 500-506, Oct., 1961. 1 fig., 11 refs.

The cases of 3 infants with an acute anaemia of haemolytic type associated with uraemia are described. The syndrome was similar to those reported by Gasser et al. (Schwelz. med. Wschr., 1955, 85, 905), and Allison (Brit. J. Haemat., 1957, 3, 1; Abstr. Wld Méd., 1957, 22, 36), and it is suggested that the syndrome may be more frequent than has been thought.

The infants were between 6 and 16 months of age. The rapid onset was accompanied by vomiting and pallor. Two patients were pyrexial and 2 had diarrhoea. Anaemia developed quickly, with jaundice in 2 cases. The blood film was typical, with well-marked anisocytosis and polkilocytosis and with fragmentation of the erythrocytes. There was some leucocytosis, with an increased lymphocyte count, and a definite thrombocytopenia. Proteinuria, haematuria, and uraemia developed in all the children, with severe oliguria lasting 5 days in one case

Treatment was with blood transfusions and 2 patients also received steroid therapy. The haemoglobin level improved immediately with transfusion. The abnormal blood cells and urine abnormalities cleared rapidly once the acute stage had passed, in 1 to 3 weeks. The blood urea level remained high for somewhat longer and then became normal in 2 of the children; in the third it did not fall below 60 mg. per 100 ml. even after discharge from hospital, although the child was clinically quite recovered.

The value of steroid therapy could not be determined in this group of cases: all 3 recovered, but only 2 received steroids. The importance of cooperation between pathologist and physician in diagnosing this syndrome is emphasized.

E. H. Johnson

473. Occurrence of *Pneumocystis carinil* Pneumonia in Children with Agammaglobulinemia

B. A. Burke, L. J. Krovetz, and R. A. Good. *Pediatrics* [Pediatrics] 28, 196–205, Aug., 1961. 6 figs., 35 refs.

Two fatal cases of pneumonitis due to *Pneumocystis carinli*, seen at the University of Minnesota Hospitals, Minneapolis, are described. The increasing incidence of this disease in North America and Britain, particularly in male infants with agammaglobulinaemia, as in the present cases, is emphasized. A morphologically similar condition is fairly commonly seen on the Continent of Europe, premature and debilitated infants being the chief victims.

The clinical picture of increasing respiratory distress and cyanosis, unproductive cough, minimal signs in the lungs, and lack of response to antibiotics was present in both cases and the pathological findings at necropsy were identical. The lungs showed extensive consolidation with interstitial infiltration by lymphocytic cells, parasites being identified in alveolar exudate. Plasma cells were not seen in significant numbers in the interstitial infiltrate (their presence is characteristic of the cases occurring in Europe) but this was presumably related to the agammaglobulinaemia. The importance of factors which alter host resistance is emphasized and staining methods are discussed. Margaret D. Baber

474. Contusion of the Lung in Childhood

A. SCHWARTZ and J. B. BORMAN. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 557-561, Oct., 1961. 10 figs., 17 refs.

The authors of this paper from Hadassah University Hospital, Jerusalem, describe the radiological and clinical features in 4 children who sustained non-penetrating blunt injuries to the chest. None of the patients had rib fractures and symptoms and signs referable to the lungs were minimal. The radiograph of the chest showed scattered or localized and irregular opacities in the lungs which might be associated with pneumothorax or haemothorax. These changes resolved within 2 to 3 weeks. All the patients were given antibiotics prophylactically. There were no pulmonary sequelae. Winston Turner

475. Nonspecific Spondylitis of Infants and Children

R. C. JAMISON, E. M. HEIMLICH, J. C. MIETHKE, and B. J. O'LOUGHLIN. *Radlology* [Radiology] 77, 355-367, Sept., 1961. 6 figs., 25 refs.

From the University of California Medical Center, Los Angeles, the authors report 6 cases of benign selflimited spondylitis occurring in 5 infants and children aged 7 months to 2½ years and one boy aged 13 years. They were all characterized by failure to identify a specific infectious agent, the mild clinical course of the disease, and recovery without the use of antibiotics. The radiological appearances were indistinguishable from those of pyogenic osteomyelitis, consisting in narrowing of an intervertebral space followed by mild destructive lesions on the adjacent surfaces of the vertebral bodies. In 2 cases an associated paravertebral softtissue mass was present. In all 6 cases spontaneous regression of the changes, with reactive sclerosis and reduction of the irregularity of the vertebral erosions, took place after 2 to 3 months. Though the narrowed disk space became wider, it never returned to its formernormal width and the affected vertebral plates showed some residual abnormality of shape.

The findings in this series are compared with those in three similar small series reported respectively by Saenger (Amer. J. Roentgenol., 1950, 64, 20), Bremner and Neligan (Brit. med. J.) 1953, 1, 856; Abstr. Wld Med., 1953, 14, 408), and Dupont and Anderson (Acta paediat. (Uppsala), 1956, 45, 361), making a total of 21 cases available for study. These showed remarkable agreement in regard to sex distribution (equal in all 4 series), age incidence (7 months to 14 years), duration of symptoms on presentation (with 2 exceptions this was never

longer than 2 months), the absence of evidence of systemic infection, and the radiographic appearances, both at the time of first examination and subsequently. The authors conclude that it is not clear whether these cases represent a new aetiological group or are merely variants of infectious spondylitis.

R. O. Murray

476. The Acute Encephalopathies of Obscure Origin in Infants and Children

G. LYON, P. R. DODGE, and R. D. ADAMS. *Brain* [Brain] 84, 427-455, Sept., 1961. 11 figs., bibliography.

From the Massachusetts General Hospital and Harvard Medical School, the authors describe 16 children who were admitted with an acute illness characterized by fever, recurrent seizures, impaired consciousness, and respiratory involvement lasting from one to several days; this syndrome has been given a variety of names, of which the authors prefer "acute toxic encephalopathy". Convulsions were present in 13 cases, but bilateral extensor plantar responses, absent pupillary reflexes, ocular motor or gaze palsies, and a decerebrate posture were less common. The cerebrospinal fluid (C.S.F.) was normal except in 2 cases in which slight pleocytosis was present, but the C.S.F. pressure was generally raised. Fever preceded or accompanied the neurological syndrome in all but 3 cases. Respiratory arrest was the usual cause of death. In 6 cases the acute illness was preceded by respiratory infection, and in another 6 by some gastro-intestinal disorder; in 3 cases no preceding illness could be identified.

In discussing the aetiology of the disorder the authors consider it possible that certain bacteria produce endotoxins harmful to the immature central nervous system. Fever appeared to be an important factor. In 3 cases the illness may have been due to electrolyte and water imbalance, resulting from excessive enteral or parenteral fluid administration, but generally this is not an important factor. Circulatory collapse and hypoxia appeared to be secondary factors. One patient, a boy aged 26 months who was admitted within an hour of onset, recovered completely. Two further patients survived the acute illness but were hopelessly demented and spastic.

Treatment should be directed towards eradication of the infection, reduction of temperature, control of the seizures, maintenance of adequate oxygenation and blood pressure, and correction of any electrolyte and water imbalance. The advantages of induced hypothermia are uncertain. The cerebral ocdema present in most cases should be reduced by administration of urea or sucrose. Post-mortem examination performed in 14 cases showed the brain to be oedematous in all but 3 in which there was hypertonic dehydration. No definite histological changes were apparent except those due to hypoxia.

H. S. Schutta ..

477. Psychomotor Seizures in Childhood: a Clinical Study of 120 Cases

J. HOLOWACH, Y. A. RENDA, and I. WAPNER. *Journal of Pediatrics* [J. Pediat.] 59, 339-346, Sept., 1961. 1 fig., 16 refs.

Medical Genetics

478. Cleft Lip and Palate: Seasonal Incidence, Birth Weight, Birth Rank, Sex, Site, Associated Malformations and Parental Age: a Statistical Survey

G. R. FRASER and J. S. CALNAN: Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 420-423, Aug., 1961.

The authors report from the M.R.C. Population Genetics Research Unit, Oxford, a statistical analysis of the sex ratio, birth weights, seasonal incidence, birth rank, and parental age of 456 child patients undergoing surgical repair of clefts of the lip and palate at the Churchill Hospital, Oxford over the past 10 years. Both hare-lip alone and hare-lip plus cleft palate showed a male: female sex ratio of about 2:1, but for cleft palate alone this ratio was less than unity (0.83:1).

Birth weights were significantly low in female patients with isolated cleft palate. No significant variation was found in seasonal incidence, contrary to the findings of Edwards (Ann. hum. Genet., 1961, 25, 83). Birth rank appeared to be important only for hare-lip alone, an analysis by sex showing an excess of patients with hare-lip alone in first-born females. An effect of parental age was seen only in the group of patients with hare-lip plus cleft palate, and here paternal age was raised more than maternal age. Analysis of birth rank and parental age combined suggested that there is an excess of elderly primiparae among the mothers of girls with hare-lip alone and of boys with hare-lip plus cleft palate.

C. O. Carter

479. The Mode of Inheritance of PTA Deficiency. Evidence for the Existence of Major PTA Deficiency and Minor PTA Deficiency

S. I. RAPAPORT, R. R. PROCTOR, M. J. PATCH, and M. YETTRA. *Blood* [*Blood*] 18, 149-165, Aug. [received Oct.], 1961. 10 figs., 9 refs.

Rosenthal et al., who first described the haemophilialike disease due to deficiency of plasma thromboplastin antecedent (P.T.A.) (Blood, 1955, 10, 120; Abstr. Wld Med., 1955, 18, 215), considered that the defect was transmitted as an autosomal dominant with a high degree of penetrance. Because of certain clinical observations, however, the present authors had doubts about a simple dominant transmission and have therefore, at the University of Southern California School of Medicine, Los Angeles, measured quantitatively P.T.A. activity in 15 patients with severe P.T.A. deficiency and in 15 of their children and 12 of their parents; similar measurements were made in 45 randomly selected normal controls.

This investigation revealed that P.T.A. deficiency may occur in two forms: (1) a major form, with P.T.A. levels of 20% of normal or less, and (2) a minor form, in which P.T.A. levels range between 20 and 65% of normal. Major P.T.A. deficiency is in general associated with a tendency to severe bleeding after surgery or dental extraction, but such bleeding is rare or much less serious in those with minor P.T.A. deficiency. The pedigrees were consistent with the hypothesis that individuals with

major P.T.A. deficiency are homozygous for an abnormal gene, which in heterozygotes results in minor P.T.A. deficiency.

H. Harris

480. Sex-linked Hydrocephalus. Report of a Family with 15 Affected Members'

J. H. EDWARDS, R. M. NORMAN, and J. M. ROBERTS. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 481-485, Oct., 1961. 7 figs., 10 refs.

The authors report from the M.R.C. Genetics Research Unit, Oxford, an extensive study of a family from Southampton in which sex-linked hydrocephalus was found to have occurred in 15 members. The index patient was a stillborn male child with hydrocephalus. and necropsy examination showed a slit-like stenosis of the aqueduct of Sylvius, a small pons, and complete absence of descending cortico-spinal tracts. Inquiry revealed that the mother had had one earlier and two subsequent stillborn males with hydrocephalus, as well as a normal boy. The pedigree shows that of more remote relatives in 2 previous generations 11 males were hydrocephalic, 3 having been stillborn, 7 dying in infancy, and one dying in 1943 at the age of 18. This last boy had been mentally defective, unable to work, and held his thumbs opposed across the palms of the hands. The distribution of the affected males in the family suggests that a sex-linked recessive mutant gene was responsible for the condition. The authors note that the present findings confirm the tentative conclusions of Bickers and Adams, who reported an almost identical case (Brain, 1949, 72, 246; Abstr. Wld Med., 1950, 7, 257), showing similar aqueductal stenosis. C. O. Carter

481. The Syndrome of Sex-linked Hydrocephalus

J. H. EDWARDS. Archives of Disease in Childhood, [Arch. Dis. Childh.] 36, 486-493, Oct., 1961. 10 refs.

The author reports three families, in addition to that described above [see Abstract 480], in which some members suffered from a syndrome showing a sex-linked recessive pattern of inheritance, the main clinical features of the syndrome being severe mental defect, a variable-degree of hydrocephalus with asymmetry of the skull and face, opposition of the thumbs across the palm of the hands, and marked spasticity of the legs with variable plantar responses.

In the first family the 2 index patients were aged 8 and 9 years respectively. One sister of the mother had a similarly affected son of 18, another sister an affected son of 13, and yet another had had 2 hydrocephalic stillborn male infants. In the second family the index patient was an adult with no affected relations. In the third family the mother had given birth to 5 affected boys, 2 of whom died in infancy, the other 3 being alive and now aged 17, 13, and 5 years respectively. This mother also had two affected younger brothers aged 38 and 32.

C. O. Carter

Public Health

482: The Nashville Air Pollution Study. I. Sulfur Dioxide and Bronchial Asthma. A Preliminary Report L. D. Zeidberg, R. A. Prindle, and E. Landau. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 489-503, Oct., 1961. 6 figs., 24 refs.

The group studied in this survey carried out under the auspices of the Vanderbilt University School of Medicine, Nashville, Tennessee, consisted of 49 adults and 35 children with "chronic bronchial asthma", a condition which is defined as being "characterized by bronchospasm and edema of the bronchial mucosa". The observations were made over the period October, 1958, to July, 1959. About half of the patients were white and half non-white, their ages ranged from 0 to 84 years, and 52% were males. A total of 123 air pollution sampling stations measuring sulphur dioxide were established throughout the study area so that no patient lived more than half a mile from an instrument. Information about asthmatic attacks was collected by means of weekly report cards maintained by the patients. Meteorological data collected included velocity and direction of the wind. temperature, humidity, barometric pressure, and rainfall. The 84 asthmatic patients reported 3,247 asthmatic attacks during the 27,440 person-days of observation, equivalent to 0.133 attacks per person per day.

For the adult asthmatics, but not for the children, the asthmatic attack rate showed a relationship to the sulphur dioxide pollution levels, being three times as high in those living in the highest of three pollution areas as in those living in the area of lowest pollution. This relationship did not clearly obtain for female adult asthmatics, however, and when the group was broken down by sex and into the three pollution areas the numbers in some were very small, for example, only one male lived in the lowest pollution area. There was no relationship between the incidence of asthmatic attacks and temperature, humidity, or barometric pressure, while wind velocity showed an inverse relationship. A fuller report is promised later.

[The small size and heterogenity of the sample and the subjective difficulty of defining and ensuring the uniform reporting of an asthmatic attack make it difficult to draw conclusions from this study.]

John Pemberton

483. Air Pollution in Road Tunnels

R. E. Waller, B. T. Commins, and P. J. Lawther. British Journal of Industrial Medicine [Brit. J. industr. Med.] 18, 250-259, Oct., 1961. 2 figs., 13 refs.

From the M.R.C. Air Pollution Research Unit, St. Bartholomew's Hospital, London, the authors report a study of the concentration of certain pollutants in the air of the Blackwall and Rotherhithe road tunnels which pass under the river Thames in east London; these tunnels are 1,490 and 1,620 yards (1,360 and 1,480 metres) long respectively. The study was carried out in the summer

months when domestic fires would be adding little to air pollution. Both diesel and petrol vehicles made some contribution to the concentration of smoke and polycyclic hydrocarbons. The amount of smoke, fluoranthene, 1:2-benzypyrene, pyrene, and 3:4-benzpyrene was more closely related to the density of diesel-engined traffic passing through the tunnel than to that of petrolengined traffic. During the rush hours the mean concentration of carbon monoxide was always over 100 p.p.m. and on one occasion reached a peak level of 500 p.p.m. Nitric oxide and nitrogen dioxide were present and eye irritation was experienced.

The authors conclude: "The concentration of pollution in the tunnels does not appear to be high enough to create any special hazards for short-term exposures. The atmosphere at peak periods may become very dirty and unpleasant and the concentration of carbon monoxide would be sufficient to produce some effect over a period of several hours' continuous exposure". They add that the total emission of pollution from road vehicles is still small in comparison with that from domestic coal fires.

John Pemberton

484. Disinfection of Woollen Blankets in Steam at Subatmospheric Pressure

V. G. Alder and W. A. Gillespie. Journal of Clinical Pathology [J. clin. Path.] 14, 515-518, Sept., 1961. 3 figs., 6 refs.

The authors of this paper from Bristol Royal Infirmary describe a method of disinfecting woollen blankets in steam at subatmospheric pressure. The apparatus consisted of a horizontal, jacketed, gravity-displacement autoclave which had recently been modernized by the addition of an oil-sealed pump and condensing unit and automatic controls. It was modified by the addition of a control valve at the steam inlet designed to close at. -10 inches (-25.4 cm.) Hg and a water ejector fitted to the chamber and jacket drains to keep the pressure on the outlet side of the steam traps below -10 inches Hg. Up to 30 hospital blankets folded lengthwise constituted a load and the chamber was evacuated to -29.25 inches (-74.3 cm.) Hg at which point steam was admitted. A temperature of 65° C. in the centre of the blankets was maintained for 30 minutes. Further evacuation to -29inches (-73.7 cm.) Hg dried the blankets, and filtered air was then admitted.

Sweep-plate cultures before and after treatment showed that vegetative organisms were consistently killed but that spore forms remained. Blankets with a pH adjusted to 4:0, 7:0, and 9:8 were disinfected 50 times with little deterioration in the physical and chemical properties.

The authors claim that the advantages of this method are speed and cheapness; it is also more pleasant for the operator than the vacuum formalin process. An old

autoclave of 25 cubic feet (0.7 c. metre) capacity could be modified for £700 and if a high pre-vacuum equipment was already fitted the cost would be as little as £150:

A. E. Wright

IMMUNIZATION AND EPIDEMIOLOGY

485. Community Spread of Orally Administered Attenuated Poliovirus Vaccine Strains

A. C. KIMBALL, R. N. BARR, H. BAUER, H. KLEINMAN, E. A. JOHNSON, and M. K. COONEY. *Public Health Reports [Publ. Hlth Rep. (Wash.)]* 76, 903–914, Oct., 1961. 1 fig., 9 refs.

This paper from the Minnesota Department of Health and University of Minnesota, Minneapolis, describes an investigation which was carried out in a crowded university village which housed 371 married students with their families. Of these, 149 (40%) volunteered to take part in the experiment and were divided into two groups of 75 and 74 families respectively, consisting altogether of 545 individuals—adults, children, and infants of both sexes. The members of one group were fed attenuated poliovirus vaccine strains and the members of the other group were given a placebo, which was indistinguishable from the oral vaccine, at the same time. Only one member of the investigating team knew the identity of the two groups while the experiment was in progress. Monovalent strains of Types 2, 1, and 3 were used as vaccines and given in that order at fortnightly intervals. Stool specimens were examined for presence of virus before vaccination and on 5 other successive occasions in the course of the experiment. The antibody response was measured by blood examination.

The authors demonstrated the spread of virus in 38 instances, involving 9 adults, 22 children, and 5 infants, or 36 persons in all. These represented 23, or about one-third, of the 74 families in the control group. There was no evidence of any illness attributable to the infection in any of these persons. Each family was usually infected by the natural spread of only one of the 3 types of virus. Type 3 showed more spread than Type 1 and the latter more than Type 2. The observed incidence of spread was equivalent to 11.3% of the total potential interfamily or community spread and was less than has been observed for intrafamily spread.

J. Caucht

486. Observations on Children Inoculated with a Live Vaccine against Poliomyelitis during the Incubation Period of Measles. (Наблюдение над привитыми живой вакциной против полиомиелата в инкубационном периоде кори)

N. D. REVENOK. Педиатрия [Pediatrija] 40, 54-59, Oct., 1961. 3 figs., 1 ref.

Oral vaccination against poliomyelitis has been proved to be safe and effective. But the question whether the virus of poliomyelitis remains genetically stable under all circumstances, especially when the child becomes feverish or has contracted measles, remains to be answered. An opportunity to study this problem occurred during a recent mass immunization programme against poliomyelitis in Moldavia in which all healthy children and

adolescents aged from 9 months to 18 years received 2 doses of the oral vaccine within 4 to 6 weeks. Soon afterwards there was an epidemic of measles in the area. Of the children who contracted measles 70% were admitted to hospital so as to be under closer observation, and these were divided into three groups as follows: (1) those inoculated against poliomyelitis during the measles incubation period (126 cases); (2) those inoculated before having been in contact with measles (135); and (3) those who had not been inoculated (252).

This study showed that the incubation period remained the same in all three groups of children. Also there were just as many children with toxic symptoms among the inoculated as among the non-inoculated. In children who developed pneumonia there was no difference between those in different groups as regards the course of that disease. Of the 2 deaths in the series neither was due to poliomyelitis but to other causes. The course of the measles did not differ in any of the children. The author therefore concludes that children who are in quarantine for measles can be safely given a live oral vaccine against poliomyelitis, and that during an epidemic of measles there is no need to withhold vaccination as long as the child is still well.

H. W. Swann

487. Trial of Living Attenuated Poliovirus Vaccine

A REPORT OF THE PUBLIC HEALTH LABORATORY SERVICE TO THE POLIOMYELITIS VACCINES COMMITTEE OF THE MEDICAL RESEARCH COUNCIL. British Medical Journal [Brit. med. J.] 2, 1037–1044, Oct. 21, 1961. 7 refs.

In 1960 an investigation was undertaken by 17 Public Health Laboratories in various parts of England to find out that system of dosage of oral live attenuated Sabin poliovaccine which would result in the greatest degree of colonization of the gut and also the best neutralizing antibody response when fed to non-immune infants. Of the 340 infants ultimately included in the trial—mostly from single-child families to reduce the possibility of natural infection-262 were aged 6 to 8 months and 78. from 9 to 11 months. At all the centres the following three vaccination schedules were employed: (I) 134 infants were given one dose of trivalent Sabin vaccine containing 1,000,000 TCD₅₀ of each of the three types of poliomyelitis virus; (II) 104 infants received 3 doses of trivalent vaccine at intervals of 4 weeks: (III) 102 infants were given 3 doses of a monovalent vaccine each containing 1,000,000 TCD₅₀-of the appropriate type of virus also at 4-week intervals, Type 1 being fed first, then Type 3, and lastly Type 2. No ill effects attributable to the vaccines were seen.

The antibody response to Type-2 virus was almost 100% in all three groups, but in Group I only about half the infants responded to virus Types 1 and 3. The best results were in Group II, in which the proportions of infants responding to Types 1, 2, and 3 were 97, 100, and 99% respectively. Triple serological responses occurred in 29% of Group II, 96% of Group II, and 83% of Group III. Colonization of the gut was again best with Type-2 virus and also best on the whole in Group II, although the best single response to Type 1, judged by antibody production and by colonization of the gut,

was in Group III, in which Type-1 vaccine was given by itself first. A certain amount of interference was observed between the three polioviruses given in the trivalent vaccine. In all three groups the antibody response was seldom satisfactory unless the virus had been demonstrated in the gut for at least a week. In infants fed the trivalent vaccine, the presence of maternal antibody in the circulation appeared to interfere somewhat with the response to Type-1 virus, but this did not occur with the other two virus types or in those given the monovalent vaccine. Spread of virus among home contacts, in the few observations made, appeared to occur more readily in children than in adults:

The antibody level in the blood after Sabin vaccine was of the same order as that after 3 doses of Salk vaccine and was well maintained 6 months after the last dose. In a small re-feeding trial with both trivalent and monovalent vaccine 6 months after the last dose it was shown that in general the virus failed to establish itself in the gut of infants who had shown a good antibody response to the original vaccine, whereas in those who had not responded, satisfactory colonization of the gut occurred uniformly. From these results, and also those reported from Soviet Russia and Czechoslovakia, it appears that in order to ensure immunity of the herd as well as the individual to poliomyelitis the Sabin vaccine is preferable to the Salk vaccine. For the sake of simplicity and ease of administration, the Sabin vaccine should be given in 3 doses of the trivalent mixture at 4- to 6-week intervals, infants being fed the vaccine by spoon or dropper and children and adults in the form of sweets.

🐪 A. Ackroya

488. The Epidemiology of the Common Cold. I. O. M. Lidwell and R. E. O. Williams. *Journal of Hygiene [J. Hyg. (Lond.)*] 59, 309-319, Sept., 1961. 4 figs., 2 refs.

This paper from the Central Public Health Laboratory, Colindale, London, forms the first of a series dealing with the epidemiology of the common cold among office workers and their families and describes the offices studied and the nature and frequency of the colds suffered by those who worked in them. The study took place in London and Newcastle and lasted from 1951 to 1957. Most of the rooms in one large Government office in Newcastle measured $72 \times 36 \times 10$ feet $(22 \times 11 \times 3$ metres); these each housed about 40 persons. 'Six to 10 rooms with a total of between 350 and 400 persons were studied each winter. From 1951 to 1954 the workers in a large commercial office in London were studied. Here rooms measuring $200 \times 200 \times 12$ feet $(60 \times 60 \times 3.8$ metres) housed about 400 people, and between 600 and 1,100 persons in 2 or 3 rooms participated in the survey. For the winter of 1954-5 records were kept of colds in two small Government offices in the north-western and southwestern suburbs of London. The rooms were of various sizes and housed from 7 to 50 persons each, the totals studied in the two establishments being 250 and 120 respectively. The study period ran from the end of August to the end of May in each year. The percentage of staff participating varied from 90 to 97. For each participant a personal record was completed and a weekly

visit was made to each subject by a nurse. Inquiry was made regarding any respiratory illness during the preceding week, and details of symptoms, onset, and duration were recorded. In Newcastle the families of those workers who lived nearby were also visited similarly.

The results showed that no useful subdivision of the common cold syndrome was possible on the basis of symptoms, although there was a significant tendency for similar symptoms to occur in colds spread among the household contacts. Colds with fever were more often associated with absence from work and were of longer duration than the afebrile. The average number of colds per year was just over 2, and 10% led to absence from work, the average duration of absence being 2.6 days. Female staff suffered 10 to 15% more colds than male staff and in the age group 30-40 years stayed away longer than males. Neither the presence of children in the household nor the daily use of public transport affected the incidence of colds significantly. The only factor found to be strongly associated with the number of colds suffered by an individual was age, infection being more frequent in the younger workers than in the older.

J. E. M. Whitehead

O. M. LIDWELL and R. E. O. WILLIAMS. *Journal of Hygiene* [J. Hyg. (Lond.)] 59, 321-334, Sept., 1961. 1 fig., 14 refs.

In their second paper [see Abstract 488] the authors have attempted to assess the importance of known contacts in the home and in the office as sources of infection for the office population studied in Newcastle. It proved possible to define separate episodes of infection in studies of families with groups of 2 to 7 individuals and thus to measure the number of infections derived from contact. In the offices this was not possible as none of the rooms held less than 20 persons and in groups of this size it was rare for no colds to be recorded in any one week. By analysing the serial interval between successive infections a median period of 21 to 31 days was found to elapse between exposure to infection and onset of symptoms. From their data the authors found that office workers with children in the household acquired 30% of their colds at home as against 10% acquired from this source by office workers with no children at home. For the entire population under study in the offices this represented about 18% of the colds acquired. They estimated that the proportion of colds mediated through contacts at work was between 5 and 30%. They thus attributed only about one-third of the colds acquired by the study population to infection from known contacts. They themselves draw attention to the limitations imposed by their method of studying the spread of infection in which only those contacts who developed symptoms could be identified as being infected. Symptomless infections and dispersal of the virus into the environment from families are suggested as possible explanations for the mode of infection in the remainder. Their data on reinfection after a cold indicated that there is reduced susceptibility for a period of at least 8 weeks.

J. E. M. Whitehead

Industrial Medicine

490. Aluminium Pneumoconiosis: a Roentgendiagnostic Study of Five Cases. [In English]

N. P. G. EDLING. Acta radiologica [Acta radiol. (Stockh.)] 56, 170-178, Sept., 1961. 7 figs., 7 refs.

The radiological findings in 5 out of 35 factory workers exposed to air containing aluminium dust are described in this paper from Karolinska Sjukhuset, Stockholm. All 5 patients showed the clinical features of aluminium dust pneumoconiosis. The mean air dust concentration varied between 4 and 50 mg. per c. metre; 4 of the patients had been exposed for 2 to 4 years and one for 13 years. When the patients moved from the dusty environment symptoms improved in 3 but continued to deteriorate in 2, one of whom died.

In 4 cases the initial fine striations or nodular rounded opacities rapidly developed to fibrosis, with pulmonary contracture and emphysema over a period of one to 2 years. After this, with one exception, little change occurred. In the exception coarse striations and massive opacities with increased pleural involvement developed, resembling to some extent the appearance in Stage-III silicosis. In the remaining case the initial changes decreased and no contracture or emphysema was evident.

The author states that the relatively mild course of the disease may be explained by the fact that aluminium particles exert a less stimulating effect on fibrous tissue formation than silica particles and are fairly rapidly "resorbed and transported from the lungs".

B. Golberg

491. A Clinical Study of Electrical Accidents W. R. Lee. British Journal of Industrial Medicine [Brit. J. industr. Med.] 18, 260-269, Oct., 1961. 21 refs.

The author, working at the University of Manchester, has studied 104 electrical accidents which happened to 85 men. He recalls that electricity may injure the body in three ways, by conversion of electrical energy to (1) light energy, which may damage the eyes; (2) to heat energy which when produced outside the body gives rise to a flash burn, or when produced in or on the body gives rise to a Joule burn, which is usually worst where the resistance is highest, that is, where the electrodes are in contact with the skin; and (3) by the passage of a current through the body, causing electric shock. Flash burns and "arc eye" were commonest in the present series, followed by electric shock and then by Joule burns. It is stated that two-thirds of the fatalities due to electrical accidents in Great Britain occur at voltages below 250.

The electric shock accidents are divided into two groups designated "not held on" and "held on", according as to whether the circuit was immediately broken or not. It is the "held on" accidents that are most likely to cause serious chest symptoms such as asphyxia and ventricular fibrillation. It is stated that

artificial respiration is the only treatment at present available to those giving first-aid, but that work is proceeding on a first-aid method of cardiac massage through the closed chest and also on a portable defibrillator.

John Pemberton

492. Leptospirosis as an Occupational Disease among, Slaughterhouse Workers in Bulgaria. (Die Leptospirose als Berufskrankheit der Schlachthofarbeiter in Bulgarien) D. MATEEW, D. KUIUMDJIEW, I. BUDUROW, and D. STOJANOW. Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. I. Abt. [Zbl. Bakt., I. Abt. Orig.] 183, 203-216, 1961. 4 figs., 13 refs.

The authors made serological examinations of the blood of 370 workers in the slaughterhouse in Sofia and found that 69 (18.6%) reacted positively against various strains of *Leptospira* as shown in the following table:

Type of Leptospira	Serologically Posi- tive in Titres of 1:400 to 1:12,800		Serologically Posi- tive in Titres of 1:100 to 1:200	
	Number	Percentage	Number	Percentage
L. pomona L. canicola L. lcterohaemorrhagiae L. pol L. saxkoebing L. australis B L. nikolaevo L. caustralis A L. sejrö Reacting with two or more types.	19 4 4 2 1 1 1 - 6	5·1 1·1 1·1 0·5 0·3 0·3 —	12 -1 1 / 2 -3 2 1 8	3·2 0·3 0·3 0·5 0·5 0·5 0·8 0·3 0·3
Total	37	. 10	32	8.6

The infection was found to be highest among the slaughterers and those concerned with the handling of carcasses of cattle and pigs. Out of 328 cattle examined serologically, 147 (44-81%) gave positive reactions against a total of 14 strains of Leptospira comprising the 9 listed in the above table, with the addition of L. ballum, L. akiyama B., L. bataviae, L. mini AB, and L. mitis. The serological examination of 240 pigs showed an even higher percentage, 163 (68%) giving positive reactions against 10 strains of Leptospira. From 184 rats and mice caught in a compound of the Sofia slaughterhouse 26 strains of L. icterohaemorrhagiae and one strain of L. sejrö were isolated.

Reference is made [without giving details] to the results of the examination of slaughterhouse workers in Burgas where 29.5% reacted positively or in a suspicious way with various types of Leptospira. Studies were also made of leptospiral illnesses in single slaughterhouse workers from various parts of Bulgaria. The results indicate that the infection is generally caught from the pigs and cattle to be slaughtered, and to a lesser extent from rats and

mice, and confirm the view that leptospiral infection is an occupational disease of slaughterhouse workers. (73 and 74% respectively) gave a history of symptoms of rheumatism and of loss of work because of rheumatism.

Edward Hindle

493. "Monday Head": an Interesting Occupational

B. W. McGuiness and E.-L. Harris. British Medical Journal [Brit. med. J.] 2, 745-747, Sept. 16, 1961. 12 refs.

It has been recognized for some time that organic nitrates can cause headache. The present authors describe 3 cases of "nitrate headache" in male chemists, aged 31, 28, and 34 years respectively, working in the development laboratory of a pharmaceutical manufacturing plant, where a new coronary-artery dilator drug, isosorbide dinitrate, was being prepared. The process consisted, basically, in the nitration with aqua regia of the dianhydro derivative of sorbitol to produce isosorbide dinitrate, which was then recrystallized from absolute alcohol. The salt, after filtration through sintered glass, was dried on trays in a vacuum oven at room temperature. The powder, when dry, was scraped by hand from the trays into glass dishes, in which it was passed to another laboratory for compounding into tablets containing lactose intended for use in experimental therapeutics in human beings.

The syndrome is characterized by a distressing headache, which may be constant and aching but which is more usually pulsatile. When severe, it is associated with "fullness in the head", palpitations, anorexia, nausea, faintness, tinnitus, mental confusion, flushing of the skin, and, occasionally, visual disturbances. The authors state that there are differing degrees of severity, the differences probably being attributable to habituation and differences in the amount of nitrate absorbed and in individual susceptibility. The headache is probably due to cerebral vasodilatation and increased intracranial pressure. The route of entry of the nitrate is through the skin or by inhalation, or possibly both. A psychic factor may be involved in the production of the headaches. The syndrome may be prevented by using pro--tective clothing, by adequate removal of dust and fumes from the workshop, and limiting, so far as possible, the amount of dust produced during milling of the material. Preventive measures are therefore a matter of elementary. industrial hygiene.

The term "Monday headache", one of the synonyms for this disorder, derives from the loss of habituation which occurs during a weekend free from exposure.

R. G. Meyer

494. Rheumatism in Cotton Operatives

J. S. LAWRENCE. British Journal of Industrial Medicine [Brit. J. industr. Med.] 18, 270–276, Oct., 1961. 2 figs., 5 refs.

The incidence of rheumatism in a sample of 117 male and 228 female cotton workers aged 45 and over was compared with the incidence in a similar number of control subjects who had never worked in cotton and who were randomly selected from an urban and rural population. More of the control subjects (89% of males and 85% of females) than of the cotton workers

(73 and 74% respectively) gave a history of symptoms of rheumatism and of loss of work because of rheumatism. On the other hand the male cotton workers had more severe osteoarthrosis in the finger and thumb joints than the controls, as assessed by radiography; it is suggested that this may be due to continuous minor traumata. The author concludes that "in view of the relatively benign nature of the disease found in cotton operatives, preventive measures are not indicated".

. John Pemberton

INDUSTRIAL TOXICOLOGY

495. Industrial Safety Experience with Trichlorethylene: Use as a Vapor Degreasing Solvent 1948–1957

J. J. HARGARTEN, G. H. HETRICK, and A. J. FLEMING. Archives of Environmental Health [Arch. environm. Hlth] 3, 461–467, Oct., 1961.

The authors report an exhaustive study of the use of trichloroethylene as a vapor degreasing solvent for the cleaning of metal, the first part of which covered the period 1948-57 while a further survey was made in 1957 to 1959. The original survey was based on studies of injuries and injury claims, statistical data on the injury-frequency rate, and on air tests in the working zones to determine the amount of exposure to which. operators were subjected. The highest annual injury figure (11 cases) occurred in 1952, when a single incident temporarily affected 7 persons. The number of deaths during the whole 10-year period was 10. The highest incidence of over-exposure necessitating medical treatment in one year (15 cases) occurred in 1953 and included 10 employees who were overcome in an attempted rescue of another workman trapped in an operating degreaser. The authors point out that the warning given by the odour and temporary nature of the effects of trichloroethylene allows many victims to recover rapidly on regaining the fresh air.

Of a total of 37 injuries and 9 deaths investigated during the period the relationship to exposure to trichloroethylene was not established or was doubtful in 29 cases of injury and in 8 of the deaths. The most frequent cause of serious injury or death was entry into a degreaser. Other causes included heating a degreaser without turning on the cooling water, accidentally falling into an open tank, overloading the capacity of the degreaser, excessive draught across it, unsafe handling of the solvent, the use of substandard equipment, inadequate room ventilation, and decomposition of the solvent.

Calculation of the injury-frequency rate, based on the number of exposure hours, gave the low figure of 0.3 injuries per 1,000,000 exposure hours. Air test surveys carried out during 1952–7 showed that the highest concentrations to which the largest number of persons were exposed occurred during the cleaning cycle, though even here in only 14% of cases was the concentration over 100 p.p.m. and in only 4% over 200 p.p.m., these values including momentary peaks. Air tests round 43 degreasers of average type showed that 93% produced concentrations less than 100 p.p.m. and none a concentration of over 150 p.p.m. This survey indicated that

normally the concentrations around trichloroethylene vapour degreasers are at a satisfactory level, and that the causes of unnecessarily high concentrations of vapour can usually be easily corrected by improvements in equipment design and safety control measures, combined with instructions designed to promote the workers' understanding of the nature of the solvent and its proper handling.

Ethel Browning

496. Health Hazards of Some Dinitro Compounds: Effects Associated with Agricultural Usage in Washington State

H. R. Wolfe, W. F. Durham, and G. S. Batchelor. Archives of Environmental Health [Arch. environm. Hlth] 3, 468-475, Oct., 1961. 6 refs.

The authors state that the health hazards to orchard workers using the sodium salt of dinitroorthocresol (Na DNOC) as a blossom-thinning spray for apples have been insignificant in the U.S.A. as compared with Europe. For weed control in America the triethanolamine and isopropanolamine salts of dinitro-o-secondary-butyl phenol (DNOSBP) are widely used as pre- and postemergence sprays, these being applied by means of wheel tractors or trucks or by aeroplane. More concentrated solutions, higher dosages per acre, and thus more days of spraying per worker are required with this compound and for this purpose than with Na DNOC. Studies of the dermal and respiratory exposure of both compounds were made, in the former case by determining the amount. absorbed by pads and cotton clothing and in the water in which the hands had been rinsed, and in the latter by examining filter pads from spray respirators. All pads, hand washes and cotton garments after extraction with water were analysed by spectrophotometry, while the urine of 14 workers with DNOSBP was also analysed.

Dermal contamination by DNOSBP, if no gloves were worn, was found to be on the average 88.7 mg. per hour, but there was considerable variation between the careful and the careless worker. DNOSBP causes persistent staining of the hands, and even after bathing and washing 2.1 and 2.8 mg, respectively were recovered from the hands of 2 sprayers. There was also considerable contamination of the lower limbs from spillage, and in warm weather, when undershirts and cotton socks were not worn, body contamination was also increased. Respiratory exposure to DNOSBP, when uncovered respirator pads were worn, was 0.47 mg. per hour, a large part of this being due to actual impingement; with pads covered with glass funnels to prevent impingement the average exposure was 0.12 mg. per hour. Truck sprayers, who sit at a lower level, received more exposure than tractor sprayers, and aeroplane sprayers less than either. Urinary excretion of DNOSBP was low, values representing an average of 22 µg. per hour being obtained. Dermal exposure to NaDNOC during blossom thinning was 24.4 mg. per hour and respiratory exposure 0.48 mg. per hour for uncovered pads and 0.03 mg. per hour for covered pads. Comparisons are drawn between British and American types of equipment and dosage and spray concentrations employed. The most - commonly used British sprayer, the reciprocating pump

machine, does not break up the spray so finely and therefore produces less drift; the dilute sprays applied in Great Britain for weed control are somewhat less concentrated and the compound used in Great Britain is more commonly DNOC, whereas in the U.S.A. the more potentially toxic DNOSBP is generally used. It is calculated that the potential exposure for a spray-man using DNOSBP for weed control would be 46% of the toxic level, while for DNOC in blossom thinning it would be 0.9%. The wearing of rubber gloves and a rubber apron is strongly recommended for the prevention of dermal exposure.

Ethel Browning

497. Clinical Contribution to the Problem of Bloodpressure Regulation and the Participation of the Heart and Circulation in Lead Poisoning. (Klinischer Beitrag zur Frage der Blutdruckregulation und der Herz- und Kreislaufbeteiligung bei Bleivergiftung)

E. Töppich and H. Minden. Archiv für Gewerbepathologie und Gewerbehygiene [Arch. Gewerbepath. Gewerbehyg.], 18, 467-478, 1961. 3 figs., 24 refs.

In view of the known spastic action of lead on the capillaries an investigation was carried out at the Clinic for Occupational Diseases, Berlin-Lichtenberg, to study the possible consequence of this action on the coronary vessels and the systemic arteries and arterioles and its relation to hypertension and cardiac involvement. It is generally agreed that during an attack of lead colic there is a rise in the systolic blood pressure, which disappears during successful treatment, and that this rise is due to a disturbance of central nervous regulation and not to a hypertensive renin mechanism resulting from spastic obstruction of the renal blood flow. The frequency. mechanism, and significance of changes in the heart and circulation were determined in 115 patients with subacute lead intoxication, all showing colic, capillary spasm, and porphyrinuria. The degree of poisoning was graded as incipient, slight, moderate, or severe according to the degree of anaemia, punctate basophilia, and porphyrinuria.

The outstanding deviation in systolic pressure was found in patients aged 16 to 24 and 35 to 54 years; the diastolic pressure was slightly raised only in the age group 35 to 44. This increase in pressure was not correlated with the severity of the poisoning and was an indication rather of the greater elasticity of the arterial system in younger persons. Its response to treatment ... indicated that it was probably not of renal origin, but due to increased liberation of adrenaline in the acute and subacute stages of lead poisoning. In only 5.2% of patients who had had no previous cardiac injury were electrocardiographic abnormalities present and these disappeared with clinical recovery; they were regarded as a typical early symptom of lead poisoning with no. serious prognostic significance. Bradycardia, with a raised T wave and S-T interval, was present in 10.9% of patients in the age group 35 to 44 and tachycardia in 3.9% in the initial stages. It is suggested that coronary infarction, though rare, is a possibility only during the acute phase of lead colic in individual cases.

Ethel Browning -

Toxicology

498. Bone Changes in Chronic Intoxication with Olephines and Vinyl Chloride. (К вопросу о костных изменениях при хронической ингоксикации олефинами и хлористым виннлом)

N. A. SMIRNOVA. Becmhux Pehmsehonosuu Paduonosuu [Vestn. Rentgenol. Radiol.] 36, 63-66, Sept.—Oct., 1961. 5 figs., 6 refs.

The author describes 3 cases of chronic intoxication with ethylene, propylene, butylene, and vinyl chlorides. The clinical picture is that of an angioneurosis. Radiographs of the hands, some of which are reproduced, showed osteoporotic zones in the distal part of the terminal phalanges. It is stated that the bone recalcifies following a change of occupation or removal from exposure to these substances.

A. Orley

499. Skeletal Sclerosis Due to Chronic Fluoride Intoxication: Cases from an Endemic Area of Fluorosis in the Region of the Persian Gulf

H. A. AZAR, C. K. NUCHO, S. I. BAYYUK, and W. B. BAYYUK. Annals of Internal Medicine [Ann. intern. Med.] 55, 193-200, Aug., 1961. 8 figs., 17 refs.

This report from the American University of Beirut, Lebanon, describes in detail 2 adult patients out of 8 who had skeletal sclerosis due to chronic fluoride intoxication acquired in Qatar on the Persian Gulf. One patient was a 40-year-old housewife with active pulmonary tuberculosis, and radiographs of the chest showed sclerosis of the ribs and clavicles. Specimens of rib were obtained during a resection of the right upper lobe and also during a partial thoracoplasty. Histologically the ribs showed marked thickening of both cortical and lamellar bone with relative diminution of the marrow space, while the osteocytes had increased considerably in number. The second patient was a 25-year-old male, also with active pulmonary tuberculosis and grand mal epilepsy. Moderate thickening of the ribs and clavicles was noted on the x-ray films, and a rib specimen was obtained during a thoracoplasty. Histologically the rib showed changes similar to those seen in the first case.

It is said that most Oatari patients show marked mottling of dental enamel with brown staining. An analysis of 14 samples of drinking water from Qatar for fluoride content showed that samples of well water contained higher concentrations of fluoride (0.79 to 3.45 p.p.m.) than those of piped water (0.8 to 1.1 p.p.m.). For comparison, in samples of drinking water from Beirut no detectable fluoride could be found. The fluoride content of the rib specimens obtained from the two Qatari patients was 20 times greater than that of 2 normal control specimens of rib. The authors point out that osteosclerotic changes due to chronic fluoride intoxication have not been observed in the U.S.A. in areas in which the fluoride concentration in drinking water is less than 4 p.p.m., but they suggest that in areas bordering the Persian Gulf certain local factors such as the hot climate and malnutrition may be responsible for the severe manifestations of this disease. They also suggest the interesting possibility that the custom of drinking tea or coffee all day long which is prevalent in many Arab countries may exaggerate the manifestations of fluorosis seen in that area, as tea is probably one of the richest sources of fluoride among the foods and beverages consumed by man.

P. T. Main

500. Hepatitis Caused by the Newer Amine-oxidase-inhibiting Drugs

C. D. HOLDSWORTH, M. ATKINSON, and W. GOLDIE. Lancet [Lancet] 2, 621–623, Sept. 16, 1961. 3 figs., 12 refs.

Liver damage carrying a high mortality is occasionally caused by the antidepressant monoamine oxidase (M.A.O.) inhibitor iproniazid, and has also been reported to occur with pheniprazine, a more recent analogue. From St. James's Hospital, Leeds, now comes this report on 4 patients, 3 female and one male, in whom toxic hepatitis due to M.A.O. inhibitors occurred on 6 occasions, the drugs concerned being pheniprazine in 3 instances, and iproniazid, nialamide, and phenelzine in first published report of liver damage resulting from nialamide and phenelzine.]

The first patient, a housewife aged 44, developed jaundice after 4 weeks' treatment with iproniazid, and 2 years later suffered another and more severe attack after receiving pheniprazine to a total dose of about 2,500 mg. over 7 months. The second patient, a woman aged 60, had an initial attack of hepatitis following doses of pheniprazine totalling about 1,500 mg., and a recurrence after receiving 1,600 mg. of nialamide over 3 weeks. In the third patient, a male aged 27, hepatitis occurred after 560 mg. of pheniprazine had been given over 60 days, and progressed despite the immediate discontinuance of the drug; the patient died one month after the onset, and necropsy showed almost complete necrosis of the hepatic cells. The fourth patient, aged 56, had an attack of hepatitis after taking phenelzine to a total of 6,300 mg, over 5 months. The duration of the jaundice in the 4 cases ranged from 2 to 9 weeks. Needle biopsy was performed in the last three cases and showed liver cell necrosis of varying severity, accompanied by infiltration of inflammatory cells in the portal tracts. [This resemblance between the histological features in drug hepatitis and those of viral hepatitis has been noted previously.] In view of the occurrence of second attacks in 2 of the patients it is recommended that treatment with another of these drugs is inadvisable once liver damage has occurred. It is also pointed out that five of . the six M.A.O.-inhibiting drugs currently in use for the treatment of depression are derivatives of hydrazine, a compound which has been shown to be hepatotoxic in J. J. Segall experimental animals.

Anaesthetics

501. Alterations in Response to Somatic Pain Associated with Anaesthesia. VII: The Effects of Nine Phenothiazine Derivatives

J. Moore and J. W. Dundee. British Journal of Anaesthèsia [Brit. J. Anaesth.] 33, 422-431, Sept., 1961. 2 figs., bibliography.

Although there is some evidence in the literature to show that chlorpromazine potentiates the action of analgesic drugs, this has not been shown to apply to all the members of the phenothiazine group. This aspect of their actions has been studied by the authors, using a method of analgesimetry in which a measurable degree of pressure is applied to the anterior surface of the tibia until the patient experiences pain.

The findings suggest a division of the phenothiazines into 3 groups as follows: (1) Those having some analgesic activity: chlorpromazine, promazine, trimeprazine. (2) Those having slight anti-analgesic action: prochlorperazine, perphenazine, trifluperazine, trifluperazine, trifluperazine. (3) Those having markedly anti-analgesic activity: pro-

methazine and pecazine.

Several unsuccessful attempts were made to correlate the above grouping with the chemical structure of the drugs. Fluorination may decrease analgesic action to some extent. The degree of analgesia produced by Group-1 phenothiazines is not as marked as that produced by pethidine.

Some of the implications of these findings have been discussed.—[Authors' summary.]

502. Prolonged Apnoéa due to Suxamethonium G. H. Bush. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 454-462, Sept., 1961. 9 figs., 37 refs.

Suxamethonium apnoea is a term which must be reserved for those cases in whom a prolonged neuro-muscular block due to suxamethonium can be demonstrated. Abnormal responses to suxamethonium mayoccur (a) following doses of the order of 1 to 1 5 g. when a dual block may develop, (b) following a single injection when the return of muscle power is delayed for approximately 10 minutes; an extended response, and (c) following a single injection when a neuromuscular block lasting 1 to 2 hours develops, a prolonged response.

Recent work suggests that the prolonged response results from failure of suxamethonium hydrolysis due to the presence of an atypical form of pseudocholinesterase, which may be recognized by the inability of dibucaine [cinchocaine] to inhibit its activity in vitro. Using this test, 3 types of persons may be distinguished; those who have only typical, those who have a mixture of typical and atypical, and those who have only atypical pseudocholinesterase. A familial pattern can be found in these persons who inherit atypical pseudocholinesterase and it is estimated that 1 in 3,000 persons will have only atypical pseudocholinesterase.

Seven cases of suxamethonium apnoea are described and in all cases the familial pattern was investigated. In 4 cases a change from depolarizing to non-depolarizing type of neuromuscular block was demonstrated and it is highly probable that this change occurs in all cases of suxamethonium apnoea. Although the apnoea is self-limiting, ventilation must be continued with a mixture of nitrous oxide and oxygen, but recovery from the non-depolarizing block can be accelerated by the use of neostigmine. The use of a test dose of suxamethonium may abolish this unnecessary and inconvenient complication of the use of suxamethonium.—[Author's summary.]

503. Studies on the Clinical and Pathological Effects of Hydroxydione

J. D. ROBERTSON and A. W. WILLIAMS. Anaesthesia [Anaesthesia] 16, 389-409, Oct., 1961. 5 figs., 25 refs.

We have found hydroxydione to be a satisfactory basal anaesthetic possessing many useful features for a variety of clinical anaesthetic procedures. However, the high incidence of local venous thrombosis in the region of the injected vein is a serious disadvantage which has not been reduced by any of the modifications in the method of administration which have been employed. From *in vitro* studies and examination of human and, animal veins which have been injected with hydroxydione, it is concluded that this thrombosis is related to chemical damage to the venous intima by the drug at the site of injection. It is suggested, therefore, that, if the advantages of this type of basal anaesthesia are to be exploited, a new method of administration is required.—[Authors' summary.]

504. Cardiovascular Effects of Phenazocine and Meperidine under Stress

E. M. GREISHEIMER, B. F. RUSY, D. W. ELLIS, and L. W. KRUMPERMAN. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 528-536, Sept.—Oct., 1961. 25 refs.

After reviewing the effects of tilting on cardiovascular physiology the authors describe a study carried out-at'. Temple University, Philadelphia, on 14 young adult volunteers. The subject was strapped to a tilting table in the horizontal-supine position and the pulse rate and blood pressure were measured after 5, 10, 11, 12, 13, 14, and 15 minutes. The subject was then tilted suddenly to the 75-degree head-up position and pulse-rate and. blood-pressure readings were taken every minute for 10 minutes. The table was then returned to the horizontal position and the subject was given either phenazocine (0.1 mg. per 7 lb., 0.16 mg. per 5 kg.), pethidine (4 mg. per 7 lb., 6.3 mg. per 5 kg.), or normal saline. Pulse rate and blood pressure were recorded 2, 4, 6, 8, and 10 minutes after the end of the injection, and the patient was then tilted 75 degrees head-up and readings

again taken. On 2 further occasions the experiment was repeated with the other 2 agents. The injections were made in random order and under "double-blind" conditions.

Impending syncope occurred on 5 occasions, all after a narcotic had been administered. It was found that tilting of the unmedicated subject produced little change in the average systolic pressure, a 20% rise in diastolic pressure, and a 27% increase in pulse rate. The administration of the 2 narcotic drugs caused little change in the pulse rate and blood pressure in the untilted subject. Upon tilting, both drugs caused a similar small gradual decrease in systolic pressure and a rise in diastolic pressure and pulse rate. The subjects who fainted showed upon tilting a marked fall in systolic pressure and marked increase in pulse rate, and were less able to maintain the diastolic pressure than those who did not faint.

Mark Swerdlow

505. Clinical Appraisal of Phenazocine: a New Analgesic as an Anesthetic Adjunct

M. S. Sadove and R. C. Balagot. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 540-550, Sept.-Oct., 1961. 6 refs.

This paper from the University of Illinois, Chicago, reports a study of the use of phenazocine ("prinadol") as a supplement to anaesthesia and for the relief of post-operative pain. Phenazocine was used as a supplement in 462 patients undergoing various surgical procedures, 65 of whom received regional analgesia. Generally anaesthesia was induced with thiopentone (average 248 mg.) and succinylcholine; intubation was then performed and anaesthesia maintained with nitrous oxide and oxygen (3:1) together with intravenous doses of 0.5 to 1 mg. of phenazocine. When muscular relaxation was necessary succinylcholine was employed. The respirations were "completely or partly controlled" in all but 80 cases.

It was found that a mean total dose of 2 to 3 mg. of phenazocine was required for procedures lasting one to 2 hours. Respiratory depression was not marked with this agent, but circulatory depression was noted in about 10% of patients who received more than a total of 4 mg. Phenazocine caused a marked diminution of pharyngeal and laryngeal reflexes.

Phenazocine was also used to treat postoperative pain, 20 patients receiving 1.5 mg. and 14 patients 2 mg. intravenously, while 6 were given 2 mg. intramuscularly. It was found that all doses gave satisfactory relief of pain, the average duration of relief being 75 to 90 minutes.

Mark Swerdlow

506. The Role of Anesthesia in Surgical Mortality R. D. DRIPPS, A. LAMONT, and J. E. ECKENHOFF. Journal of American Medical Association [J. Amer. med. Ass.] 178, 261–266, Oct. 21, 1961. 6 refs.

The role of anesthesia in contributing to surgical mortality has been studied in 33,224 patients given either spinal anesthesia or a general anesthetic to which muscle relaxants were added. There were no deaths attributable to anesthesia in the 16,000 physically fit patients anesthesia.

thetized by either technique. As the patients' physical condition worsened, deaths related to anesthesia increased in incidence; in the moribund patients, 1 in 16 patients given spinal anesthesia died of causes related to the anesthetic, and in 1 in 10 patients, general anesthesia could not be excluded as contributing to death. Of 6,000 physically fit patients who received a muscle relaxant, none died. No evidence of an inherent toxicity of muscle relaxants could be found. When deaths were related to the use of muscle relaxants, errors of omission or commission were apparent.—[Editorial summary.]

507. Postoperative Procedure to Control Pain of Patients Reacting from Light Planes of Anesthesia

L. M. Monheim and A. J. Fisher. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 404-407, July-Aug., 1961. 7 refs.

The use of intravenous barbiturate muscle relaxants and nitrous-oxide—oxygen anaesthesia has permitted of lighter planes of anaesthesia. The consequent shortening of recovery time, however, sometimes to 30 minutes after the end of the operation, has meant that more patients complain of postoperative pain. An investigation of the use of pethidine and promethazine for relief of such pain was therefore carried out at the Presbyterian and Women's Hospitals, Pittsburgh.

In the first part of the study 300 patients were premedicated with pentobarbitone or quinalbarbitone, with promethazine and either atropine or scopolamine, and anaesthetized with thiopentone, nitrous oxide, and oxygen. One half of the patients were then given 50 mg. of promethazine hydrochloride together with 50 mg. of pethidine by intramuscular injection 20 to 30 minutes before the termination of surgery, the remaining 150 (control) patients being "handled in the usual routine manner" postoperatively. Of the treated patients 147 had a quiet pain-free emergence from anaesthesia, whereas 37 of the control group exhibited severe pain and restlessness on recovery.

In the second part of the study 512 patients received the same premedication and anaesthesia as above, but were given no analgesic agents until they complained of postoperative pain, whereupon an intramuscular injection of 50 mg. of promethazine plus 50 mg. of pethidine was given. Of the 147 patients who complained of severe pain 124 (85%) obtained complete relief; of the 353 with moderate pain 349 (99%) obtained relief, while all 12 patients with mild pain were completely relieved. Relief of pain occurred within 25 to 35 minutes of injection and lasted 1.5 to 12 hours (average between 2 and 4 hours). Relief of pain was accompanied by extreme drowsiness or sleep.

[It would have been interesting to know something about the type of operations performed and the nature of the "usual routine manner of postoperative medication".]

Mark Swerdlow

508. The Performance of a Walton Five Anaesthetic Machine

W. D. A. SMITH. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 440-453, Sept., 1961. 16 figs., 5 refs.

Radiology

509. Leukemia in Radiologists, Ten Years Later: with a Review of the Pertinent Evidence for Radiation Leukemia H. C. MARCH. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 137-149, Aug., 1961. Bibliography.

The mortality rate for leukaemia among radiologists in the U.S.A. during the decade 1949 to 1958 was estimated to be 3·23%. This was somewhat lower than the comparable figure (4·68%) for the preceding 20 years but was still considerably higher than the mortality (0·51%) among physicians who were not radiologists. The author of this paper from the University of Pennsylvania, Philadelphia, states that it is anticipated that with awareness of the problem and adequate precautions by radiologists this differential will tend to diminish but will not entirely disappear.

The evidence suggesting a causal relationship between exposure to ionizing radiation and the development of leukaemia is reviewed. The most positive evidence supporting this comes from the experimental induction of leukaemia in animals, from the data obtained from the population exposed to the atomic bombing of Hiroshima and Nagasaki in 1945, and from the higher incidence of the disease among radiologists and patients given radiotherapy for ankylosing spondylitis. Most of the evidence suggests a linear dose—response relationship in radiation-induced leukaemia, but whether this holds for small doses or whether there is a threshold dose remains an unsettled problem.

L. A. Elson

RADIODIAGNOSIS

510. Contrast Examination of Larynx and Pharynx: Accuracy and Value in Diagnosis

W. E. POWERS, S. HOLTZ, J. OGURA, B. L. ELLIS, and M. H. McGAVRAN. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 651-660, Oct., 1961. 8 figs., 5 refs.

Since the method to be employed in treating laryngeal or laryngopharyngeal carcinoma depends on the location. size, and extent of the tumour, a reliable and accurate evaluation of these factors is essential. Contrast radiography, which will define the tumour masses and show evidence of functional impairment, is simple, accurate, and safe. It is more valuable than tomography, alone or combined with a barium swallow, and from the radiographs it is possible to observe the response of the tumour to irradiation and the functional result afterwards. The patient is prepared with atropine and pentobarbitone, and a local anaesthetic is sprayed into the pharynx and dropped into the larynx. During quiet inspiration 10 to 20 ml. of oily "dionosil" (propyliodone) is dropped slowly over the tongue. Frontal and lateral spot radiographs are taken during nasal inspiration, phonation, and

modified and true Valsalva manœuvres. This procedure is carried out before a biopsy specimen is obtained so that oedema will not distort the anatomy.

The authors of this paper from Washington' University School of Medicine, St. Louis, Missouri, have reviewed the records of 99 out of 170 patients in whom laryngography was carried out during the period 1957-9. The accuracy of laryngography proved to be high, 92% correct evaluations as compared with 78% by conventional clinical appraisal. The majority of the errors occurred in the infraglottic group, due to an enlarged true cord and infraglottic mass impressing and almost obliterating the ventricle. Because of the incorrect interpretation of false-cord involvement these cases were classified as cases of transglottic lesions. In bulky supraglottic tumours it was possible to demonstrate the freedom of involvement. of the true cords. The authors state that by laryingography the tumour size can be evaluated within a mean variation of 0.3 to 0.6 cm. depending on the tumour site. Laryngography was not designed for the appraisal of lesions in the post-cricoid region, where a barium swallow is necessary. John H. L. Conway-Hughes

511. Circumscribed Intrapulmonary Haematoma

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E. MILNE and A. DICK. British Journal of Radiology [Brit. J. Radiol.] 34, 587-595, Sept., 1961. 6 figs., 16 refs.

Although they could find only 9 cases of circumscribed pulmonary haematoma in the literature, the authors were able to collect 6 new cases in 8 months during a review of closed thoracic injuries at the Royal Infirmary, Edinburgh. From a study of this material they conclude that usually the injury is of a crushing type or a glancing blow from a blunt instrument or surface, and the subject a young man under 30. Radiological examination of the chest within a few hours reveals an ill-defined opacity at the site of the injury extending to the pleural surface, and often wedge-shaped with the apex towards the hilum. The opacity may become extremely dense over the next few days and increase in area. From 3 days to 6 weeks (usually about 7 days) after the injury the consolidation becomes condensed and circumscribed, and displays a fluid level within it in most cases (5 out of 6 cases in the authors' own series). Serial radiographs show gradual shrinkage of the haematoma over a period of 3 weeks to 44 months. B. Golberg

512. Nerve Root Radiography

K. Bleasel. British Journal of Radiology [Brit. J. Radiol.] 34, 596-601, Sept., 1961. 17 figs.

This paper describes a variation in the technique of myelography which has been used at Lewisham Hospital, Sydney, Australia, for the investigation of lesions of the cauda equina and nerve roots of the lumbar and sacral regions. The variation involves the emulsification of "myodil" (ethyl iodophenylundecylate) in the cerebrospinal fluid so that it becomes more translucent to x rays and capable of demonstrating nerve roots. The advantages of the method as applied to the lumbar sac are stated, but there are insufficient data to assess the value of the technique for higher levels above the conus medullaris.

The myodil appears to re-form into a single mass within days of the injection. The emulsion is formed by shaking 6 ml of myodil in a 20-ml all-glass syringe with 14 ml of cerebrospinal fluid and a bubble of air. The mixture separates into a layer of froth, a layer of almost clear supernatant fluid, and approximately 8 ml of myodil in the form of a cloudy emulsion. The upper two layers are discarded and the 8 ml of myodil suspension is injected into the lumbar sac.

It is suggested that the more translucent myodil suspensions can indicate the course of nerve roots before they enter the sheaths. Posterior compression may be recognized and a complete block due to tumour may be distinguished from one which is due to central disk protrusion.

J. Mac D. Holmes

513. Comparison of Intraosseous Vertebral Venography and Pantopaque Myelography in the Diagnosis of Surgical Conditions of the Lumbar Spine and Nerve Roots

R. A. SCHOBINGER, E. G. KRUEGER, and G. L. SOBÈL. Radiology [Radiology] 77, 376-398, Sept., 1961. 15 figs., bibliography.

The disadvantages of myelography in the routine investigation of suspected disk prolapse and other spinal conditions can be avoided by greater use of vertebral venography, the technique of which is as follows. After suitable sedation the patient is placed in the prone posi-. tion with a narrow compression band over the lumbar spine and under the lower abdomen an inflatable rubber bag the inflation of which will temporarily compress and occlude the inferior vena cava. Under local anaesthesia a 16-gauge Rosenthal bone-marrow needle is inserted into the spinous process and its position checked by aspirating blood containing marrow particles. An injection of 2 to 3 ml. of 2% procaine is given, the inferior vena cava is compressed, and 25 ml. of 50% sodium diatrizoate is then injected manually in 5 seconds. A single postero-anterior radiograph is taken near the end of the injection, but lateral and oblique views can also be helpful.

The authors of this paper from Columbia University, New York, and associated hospitals have examined 68 patients by this method. They report two failures only, due to extravasation or injection of the medium into the epidural space, which can be avoided by careful adherence to the technique. In the normal subject the continuous pattern of epidural veins and other venous structures which is bilaterally symmetrical is demonstrated. Prolapsed disks compress and displace the epidural veins and a collateral circulation develops; spinal metastases interrupt the flow completely with no collaterals, and these changes may be present when conventional radiographs and tomograms are normal. An

intradural tumour (2 cases) produced compression and displacement of the epidural veins.

It is concluded that while venograms are more difficult to interpret than myelograms they are more reliable in the diagnosis particularly of disk protrusions and spinal metastases. Venography can safely be employed as a routine procedure, myelography being reserved for cases in which it is really needed.

D. E. Fletcher

514. Antegrade Aortography and Arteriography. Furthur Experience with the Method. Its Place in Arterial Opacification Technics

L. C. Hamilton and W. V. Weldon. Radiology [Radiology] 77, 406-417, Sept., 1961. 10 figs., 14 refs.

An investigation was carried out at the Walter Reed Army Medical Center, Washington, to determine the value of antegrade arteriography in demonstrating lesions of the aorta and its branches. Catheterization of the right auricle was carried out in the usual manner in 125 patients and 90% sodium diatrizoate in a dosage of 12 ml. per kg. body weight was used as the contrast material with automatic injection pressure of 10 kg. per cm. Circulation time from the atrium to the tongue was determined with "decholin" and from the atrium to the popliteal artery with diodone labelled with radioactive iodine and a scintillation counter.

The detail afforded did not equal that obtained by the best retrograde techniques but was quite acceptable for the aorta and its main branches. Renal artery stenosis was demonstrated in 10 out of 38 hypertensive patients, the remainder being normal. The carotid and vertebral arteries were reasonably demonstrated, the aortograms probably being adequate for occlusive disease in the neck. The method is one which requires special apparatus and a trained team. It is, however, much safer and easier to perform than the retrograde technique with its risks of arterial thrombosis, embolism, and haematoma.

, D. E. Fletcher

515. Diagnostic Radiology of the Femoro-patellar Joint and Its Clinical Significance. (Die Röntgendiagnostik des Femoropatellargelenkes und ihre klinische Bedeutung)

D. Andersen, F. Baumgartl, and H. Gremmel. Radiologe [Radiologe] 1, 216-222, Oct., 1961. 11 figs., 17 refs.

At Düsseldorf Medical Academy the authors have. studied the radiological appearance and position of the patella in relation to clinical disorders of the knee-joint. They find that, as seen in the axial view, the patella is often very unevenly developed, as was previously reported by Wiberg (Acta orthop. scand., 1941, 12, 319). Frequently, owing to maldevelopment of the medial facet. the patella does not cover both condyles of the femur. equally, additional strain then being thrown on to the lateral side of the knee-joint which leads to an increased tendency to develop intra-articular effusion. The presentauthors concur with Wiberg's recognition of 3 types of patella-Type I, in which both facets are equal in size, Type II (the normal type), in which the medial facet is smaller than the lateral, both being concave, and Type III, in which the medial facet is still smaller than in Type II.

and has a convex inner surface. They also recognize an intermediate type, Type II/III, in which surface of the medial facet is flat, and an extreme form of this intermediate form, in which the medial half of the patella is virtually absent and which has been named the Jägerhut type. Finally they describe a very rare type, Type IV, in which the medial facet has an irregular surface and which is associated with osteochondritis dissecans.

They found the distribution of types of patella among subjects with normal knees to be: Type I, 11%; Type II, 55%; Type II/III, 23%; and Type III, 11%. Among 50 knees with recurrent effusion the corresponding distribution was 0%, 9%, 48%, and 43%.

F. M. Abeles

516. The Indication for Direct Enlargement Technique in Bone Radiography. (Die Indikation zur direkten Röntgenvergrösserung bei Knochenaufnahmen)
H. BÜCHNER. Radiologe [Radiologe] 1, 222-229, Oct., 1961. 20 figs.

The author discusses the theoretical basis and practical results of the use of enlargement techniques in the radiography of bones. He concludes that considering all circumstances an enlargement technique invariably gives inferior results, and its use is not recommended.

F. M. Abeles

517. Retrograde Colonic Spread of Enemata in Ulcerative Colitis

S. G. F. MATTS and K. H. GASKELL. British Medical Journal [Brit. med. J.] 2, 614-616, Sept. 2, 1961. 6 figs., 7 refs.

A radiological investigation has been conducted into the degree of penetration of intrarectally introduced solutions into the colon. This shows that penetration can sometimes be achieved as far as the ascending colon with only 100 ml. of radio-opaque suspension. In most sufferers from ulcerative colitis, the left side of the colon can easily be reached. No significant difference was shown between the slow drip and the single-dose plastic-enema-bag method of administration. In people not suffering with ulcerative colitis the degree of retrograde spread was less. Reasons for this are briefly discussed. Ulcerative colitis by its nature therefore seems to lend itself to intrarectal therapy.

The significance of the degree of penetration of intrarectal solutions is briefly discussed with respect to the plastic-bag evacuant enemata used in many nursing procedures.—[Authors' summary.]

- 518. The Roentgen Findings in Lymphosarcoma of the Small Intestine

R. H. MARSHAK, B. S. WOLF, and J. ELIASOPH. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 682-692, Oct., 1961. 11 figs.

The radiological changes in 75 proved cases of primary lymphosarcoma of the small intestine investigated at the Mount Sinai Hospital, New York, were divided into 5 main categories, as follows.

(1) Multiple small nodular defects within the lumen; these defects after the mucosal pattern and produce an irregular coarse scalloping of the bowel contour, but the bowel is not narrowed or fixed, and retains its pliability. Such changes are usually found in the ileum, and may involve segments up to 2 ft. (60 cm.) in length. This form may also be accompanied by other changes in the small or large intestine. In the present series 5 cases of this type were seen, in 3 of which there was colonic involvement as well. (2) The infiltrating form, in which the intestinal wall becomes diffusely infiltrated and thickened for considerable lengths and to a varying degree, so producing irregular segments of narrowing and relative dilatation: the narrowing is never so marked as in carcinoma or inflammation of the intestine. The mucosal folds may be flattened or thickened into irregularnodular projections, producing coarse irregular scalloping of the bowel contour with varying intraluminal filling defects. The mural thickening causes separation and straightening of the bowel loops. Marked rigidity of involved segments does not occur, nor is there sufficient, stenosis to cause proximal dilatation. Marked localized or "aneurysmal" dilatation may occur in short lengths segmentally infiltrated.

(3) The polypoid form. When a discrete intraluminal mass, without intramural extension, is large enough it may become the apex of an intussusception: the polypoid tumour is rarely visualized in such a case. In 4 of the authors' patients intussusception alone occurred, while in 3 others additional evidence of such involvement was present. (4) The endo-exocentric form with cavitation; in this form a large excavated mass occurs, with multiple fistulae and communications with the small intestine. At an early stage the involved portion of the small bowel may be criss-crossed by many intercommunicating channels connecting the tumour with the lumen of the small. intestine; at a later stage, however, the adjoining loops of intestine are displaced by the large mass. These appearances may also be produced by other sarcomatous tumours of the intestinal tract. (5) The predominantly invasive form, of which there are two types: (a) Large extraluminal masses may extend retroperitoneally, causing displacement of other organs and invading the intestinal wall; in this type intestinal obstruction is infrequent. (b) The sprue pattern may be produced (associated with typical clinical and laboratory findings) when there is diffuse involvement of the mesentery; 8 cases of this type were seen, while in a further 2 there was also evidence of extraluminal masses.

The differential diagnosis from Hodgkin's disease, multiple polyps, infarction, carcinoma, and carcinoid and regional enteritis is discussed.

B. Golberg

519. Rocatgen Diagnosis of Lymphosarcoma and Reticulum Cell Sarcoma in Infancy and Childhood

R. S. SHERMAN and S. L. WOLFSON. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 693-701, Oct., 1961. 8 figs., 31 refs.

The records of 60 cases of lymphosarcoma or reticulumcell sarcoma occurring in patients under 12 years of age seen at the Memorial Sloan-Kettering Cancer Center, New York, in the period 1928 to June, 1958, have been reviewed. After exclusion of the 23 patients who developed leukaemia the 37 cases without evidence of leukaemia were studied, these consisting of 24 cases of lymphosarcoma, 12 of reticulum-cell sarcoma, and one of follicular lymphosarcoma.

In only 4 patients, all of whom had local disease in the neck, were the results of radiological examination negative. Of the others, 9 showed involvement of bone, in 2 cases consistent with primary reticulum cell sarcoma, 2 showed generalized changes similar to those seen in leukaemia, and in 2 others there were single osteolytic deposits. Bilateral and roughly symmetrical enlargement of the kidneys was present in 6 out of 8 patients with known renal involvement; in one of these a localized defect with calyceal deformity was present. Enlargement of both the liver and spleen was observed radiographically in 3 cases and separately once each. Radiological evidence of lymph-node enlargement was present in 50% of the cases, usually in the mediastinum, and less frequently in the abdomen. The presence of abdominal fluid was suspected in 7 cases, pleural effusion in 5, and in 4 fluid was thought to be present in both cavities. Ten patients showed one or more areas of lymphosarcoma in the gastro-intestinal tract, this being usually polypoid and infiltrating in character; intussusception occurred in 6 patients. Lesions were found in the lungs of 5 patients, while other sites affected included the nasopharynx, ovary, mandible, sphenoid bone, and duodenum.

The authors discuss fully the differential diagnosis of lymphosarcoma from leukaemia, Hodgkin's disease, neuroblastoma, and Wilms's tumour and note the multiple sites of involvement and their irregular sequence and haphazard arrangement in the body which characterize lymphosarcoma.

B. Golberg

520. Angiography in the Diagnosis of Renal Carcinoma. [In English]

E. Bousen and J. Folin. Radiologe [Radiologe] 1, 173-191. Sept., 1961. 24 figs., 11 refs.

This paper from the University of Lund, Sweden, presents a comprehensive discussion of the value of angiography in the diagnosis of renal tumours. It is based on 84 personal cases, about half of which were investigated by selective renal angiography and half by aortic angiography. The authors pay particular attention to narrowed arteries, and also to the minute arteries supplying the renal capsule and renal pelvis. They next deal with the question of multiple renal arteries, as related to either angiographic method; with selective renal angiography no filling is obtained of supplementary arteries and resort to aortic angiography may be necessary. The value of the late arterial phase is stressed, and this is followed by a full discussion of the nephrographic phase.

Finally, consideration is given to the venous phase, which is mainly important in deciding whether the veins have really been invaded by the tumour or whether they have only been compressed or displaced by it. Occasionally in such cases special venograms are required.

F. M. Abeles

521. The Lower Urinary Tract in Infants and Children L. A. DAVIS, R. LICH, L. HOWERTON, and W. JOULE. Radiology [Radiology] 77, 445-451, Sept., 1961. 9 figs., 14 refs.

The presence of urinary tract obstruction in children is not always detected by routine intravenous pyelography; a complete examination of patients with chronic infection must include micturating cysto-urethrography. The technique adopted at the Children's Hospital, Louisville, Kentucky, is as follows. A catheter is passed into the bladder and 20% sodium diatrizoate is injected by hand while the bladder is monitored by the image amplifier. The amount injected varies from 1 oz. (28 4 ml.) in the newborn infant to about 6 oz. (170 ml.) in children aged 3 to 5 years and 8 to 10 oz. (227 to 284 ml.) in older children. The catheter is removed and up to 12 serial radiographs of the urethra are taken, in males usually in a semi-oblique position.

Of 308 children examined by this method some abnormality was found in 137, including ureteric reflux, diverticula of the bladder, obstructive lesions of the bladder neck, urethral valves, and ectopic ureter.

D. E. Fletcher

RADIOTHERAPY

522. Radiation Myelopathy.
C. A. Pallis, S. Louis, and R. L. Morgan. *Brain* [*Brain*] 84, 470–489, Sept., 1961. 2 figs., 19 refs.

Thirty-eight previously reported cases of radiation myelopathy are reviewed with regard to early symptoms and signs, differential diagnosis, prognosis, nature of the primary lesion irradiated, and latency between irradiation and the development of neurological symptoms. A further 5 cases are described, including one in whom a hitherto unrecorded feature was observed, namely the association of myelopathy with radionecrosis of the overlying bone.

The pathological basis of radiation myelopathy is briefly reviewed. The difficulties in estimating the radiation tolerance of the human spinal cord are discussed and some facts are presented in relation to the incidence of radiation myelopathy in patients with irradiated bronchial and postcricoid carcinoma.

On the basis of a review of all previously reported cases and of our own material, new limits are proposed for the dose of radiation which may safely be tolerated by the human spinal cord.—[Authors' summary.]

523. The Roentgen Therapy of Pontine Gliomas

J. S. REDMOND JR. American Journal of Roentger

J. S. REDMOND JR. American Journal of Roentgenology; Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 644-648, Oct., 1961. 1 fig., 14 refs.

In this paper are presented the results of x-ray therapy in 42 patients with pontine gliomata seen from 1936 to 1959 at Duke University Medical Center, Durham, North Carolina. Of these, 29 were in the 3 to 10 age group and the eldest was aged 53. Headache was the most common initial symptom, but abnormal gait was commonest when the patients were first seen. Sensory changes were found to be rare in contrast to motor changes. Plain radio-

graphs were abnormal in 13 cases, and ventriculography was considered diagnostic in 18 of the 23 cases in which it was performed. Since the late 1940's ventriculography has been part of the standard investigation of these cases. In the remainder the diagnosis was based on characteristic clinical findings. The dangers of biopsy in pontine glioma are mentioned; in the present series it was performed in only 2 out of 8 cases treated surgically.

Of the 42 cases, 30 received at least one course of irradiation at 200 to 240 kV. peak, most cases being treated with two opposing fields and one posterior field. Twelve cases received doses of 3,000 to 4,000 r. and 12 cases doses of 2,000 to 3,000 r., usually in 3 to 4 weeks. Most patients died in the first year after treatment, but in 12 cases there was considerable clinical improvement and in 8 moderate improvement. The results are tabulated against dose, and it is suggested that doses of less than 2,000 r., and probably those of less than 3,000 r., were below the optimal range. The author hopes for better results from the use of higher-energy sources and higher doses.

E. D. Jones

524. Acthomycin D and Roentgen-ray Therapy in the Treatment of Metastatic Wilms' Tumor

D. H. ALTMAN. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 673-681, Oct., 1961. 13 figs., 4 refs.

The results obtained with a combination of actinomycin D and irradiation in 5 cases of Wilms's tumour and metastatic disease seen at the Variety Children's Hospital or Jackson Memorial Hospital, Miami, Florida, are described. Usually the patients received $75\,\mu\mathrm{g}$ of actinomycin D per kg, body weight divided into 5 daily doses. The author states that in 2 patients with metastatic disease treated primarily with actinomycin D there was moderate palliation and that the best results were obtained by initial concomitant administration of actinomycin D and radiotherapy. The history and treatment of each case are detailed and serial radiographs in 4 of the cases are reproduced, the 13 figures including 23 such radiographs.

525. Malignant Tumours of the Buccal Cavity: a Clinical Analysis of 970 Cases

S. K. BHANSALI. Clinical Radiology [Clin. Radiol.] 12, 299–308, Oct., 1961. 1 fig., 6 refs.

Nine hundred and seventy cases of malignant tumours of the buccal cavity have been analysed. Over one-fifth of the lip cancers and more than one-half of the other buccal cavity tumours had metastasised to regional lymph nodes when first seen. Most of the tumours were squamous carcinomas. Nearly one-fourth of the tumours arising from the hard palate were malignant sialomas. The incidence of multiple primary tumours was 12%. One-third of the second tumours occurred in the buccal cavity. The incidence of buccal cavity cancer is decreasing and the proportion of women is becoming greater.

Tumours of the lip have an overall 5-year net survival rate of .76%. At other sites the results are roughly

uniform and about one-third of the net cases survive for 5 years. At the present time a combination of radio-therapy and surgery appears to hold out the best hope for the patient. Regional lymph node involvement is of serious significance. About one-fourth of the "node free" patients develop lymph node metastases within 3 years, and prognosis in these cases is almost as bad as those in which lymph nodes are involved when the patient is first seen. In the absence of regional lymph node metastases the survival rate shows a four-fold improvement. The prognosis in females is better than that in males. The results in the period 1946 to 1955 are better than those in the period 1936 to 1945.—[Author's summary.]

526. Preoperative Irradiation in Rectal Carcinoma R. H. LEAMING, M. W. STEARNS, and M. R. DEDDISH. Radialogy [Radialogy] 77 257-263 Aug. 1961 1 fig.

Radiology [Radiology] 77, 257–263, Aug., 1961. 1 fig., 5 refs.

The authors review all patients (1,276) with rectal or recto-sigmoid carcinoma operated upon at the Memorial Center, New York, between 1939 and 1951. The overall 5-year survival rate was 37.4% and for those patients (971) whose growths were resected it was 49%. Of the 1,276 patients, 727 (57%) were given preoperative x-ray therapy [but the authors do not indicate how these were selected]. Of the patients whose growths were resected, 51% had had preliminary radiotherapy.

Irradiation was given at 200 kV. with H.V.L. 1 0 mm. Cu and F.S.D. 70 cm., 2 anterior, 2 lateral, and 2 posterior fields, each 14×11 cm., being used. The dose (in air) to the anterior fields was 450 r. and to the others 900 r. For tumours within 8 cm. of the anal verge a 10-cm, perineal cone was added, with slightly different factors. - The daily dose (in air) was 450 r. and the total treatment time 2 weeks. With the 6-field technique the maximum tissue dose was 1,200 r: and the minimum tissue dose 800 r. When the perineal field was added an additional 450 r. was delivered to the tumour. Operation did not always follow at once, the interval being under one month in about 25% of cases, 1 to 3 months in about 60%, and over 3 months in the remainder. [There is some discrepancy between the sum of the group totals and the over-all total as given in the authors' table from which this information is extracted.]

From an analysis of the results the authors conclude that although no beneficial effect from radiotherapy could be demonstrated in cases without lymph-node involvement, an important and statistically valid improvement was evident in those in which the nodes were involved (Dukes's Stage C). Of 395 Stage-C cases, preoperative radiotherapy was given in about 50% and the 5-year survival rate was thereby raised from 25% to 43% of determinate cases. The authors therefore make a plea for routine preoperative irradiation in cases of rectal carcinoma and state that at the Memorial Center cases are now being selected on a random basis for this treatment. They feel confident that improved supervoltage techniques now being used will show even better results.

E. Stanley Lee .

ABSTRACTS OF WORLD MEDICINE

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Pathology

[In

527. Histamine Formation in Human Blood.

S. E. LINDELL, H. RORSMAN, and H. WESTLING. Acta allergologica [Acta allerg. (Kbh.)] 16, 216–227, 1961. 17 refs.

Basophil granulocytes are the main carriers of blood histamine in man. The authors of this paper from the University of Lund and the University of Gothenburg, Sweden, describe experiments to determine whether human basophils are merely carriers of histamine or whether they can also synthesize it. The rate of histamine formation from histidine labelled with radioactive carbon in vitro was examined in blood samples from normal subjects and from patients with myeloid and lymphatic leukaemia, polycythaemia, eosinophilia, and urticaria pigmentosa. It was found that there was a significant correlation between the number of mature basophil cells and the rate of histamine formation.

A. W. Frankland

528. Evaluation of the Radioactive Rose-bengal Test for the Differential Diagnosis of Obstructive Jaundice in Infants

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H. GHADIMI and A. SASS-KORTSAK. New England Journal of Medicine [New Engl. J. Med.] 265, 351-358, Aug. 24, 1961. 2 figs., 20 refs.

In young infants the differentiation between obstructive jaundice resulting from atresia of the extrahepatic bile ducts and obstructive jaundice due to intrahepatic conditions with patent extrahepatic bile ducts is a difficult diagnostic problem but one of great importance, since in the former case surgical correction within the first 4 weeks of life is mandatory if irreversible changes in the parenchyma of the liver are to be avoided. Working at the Hospital for Sick Children, Toronto, the authors have confirmed that ¹³¹I-labelled rose bengal (1 µc. in 1 to 10 mg. of carrier) injected intravenously was excreted in the 72-hour stools of 4 patients with patent extrahepatic biliary ducts in twice the concentration, or more, of that in similar specimens from 7 infants with biliary atresia, the values in the two groups being 10.5% and 2.2 to 5%of the injected dose respectively. The rose bengal test is thus likely to provide valuable information regarding the need for surgical intervention in affected subjects. The risk of radiation damage to the gonads or thyroid gland, which is shown to be much less than, for example, that for a one-minute fluoroscopic abdominal examination, may be minimized by pretreatment with Lugol's iodine. M. Sandler

529. The Nature of the Fibrinolytic-enzyme Defect in Hyaline-membrane Disease

J. LIEBERMAN. New England Journal of Medicine [New Engl. J. Med.] 265, 363-369, Aug. 24, 1961. 2 figs., 30 refs.

In a previous paper (New Engl. J. Med., 1959, 260, 619; Abstr. Wld Med., 1959, 26, 193) the author had demonstrated a lack of plasminogen-activator in the lungs of infants dying from hyaline membrane disease. In this further study reported from the University of California Medical Center, Los Angeles, he has now been able to show that this significant decrease in activator activity is due to the presence of a specific inhibitor of such activation which adheres to particulate matter containing the enzyme. Since high concentrations of this inhibitor were detected in homogenates of placental tissue-theauthor suggests that placental infarction, as occurs in some patients in premature labour or with diabetes mellitus, may release the inhibitor into the foetal circulation, so preventing the dissolution of intra-alveolar fibrin and thus leading to the subsequent formation of hyaline membrane. M. Sandler

HAEMATOLOGY

530. Studies on the Fetal Hemoglobin in the Persistent High Hb-F Anomaly

R. B. THOMPSON, J. W. MITCHENER, and T. H. J. HUISMAN. *Blood* [*Blood*] **18**, 267–284, Sept., 1961. 5 figs., 33 refs.

"It is well known that foetal haemoglobin occurs in large quantity in the blood of new born children." Normally it disappears within a few months after birth, but increased values are found with some regularity in a number of haemoglobinopathies such as thalassaemia and sickle-cell disease: There is a condition in which there is no anaemia but in which foetal haemoglobin persists into adult life, and this persistence has been found to be hereditary.

The present paper, from the Medical College of Georgia, Augusta, reports a chemical and genetical study of this foetal haemoglobin. It has been found to be in no way different from the foetal haemoglobin of the newborn, and by histochemical tests it was possible to demonstrate that it was equally distributed among all the cells of those affected. In this respect the condition differs from sickle-cell anaemia, in which haemoglobin F is found in some cells but not in all. H. Lehmann

 Coagulation Tests on Capillary Blood: a Screening Procedure for Use in Small Children

K. M. DORMANDY and R. M. HARDISTY. *Journal of Clinical Pathology* [J. clin. Path.] 14, 543-547; Sept., 1961. 5 figs., 9 refs.

The authors of this paper from the Hospital for Sick Children, Great Ormond Street, London, point out that while investigations of clotting mechanisms are best carried out on blood obtained rapidly by clean venepuncture, such specimens may be difficult to obtain in children. They describe a procedure by which routine investigation of coagulation may be performed on 0.2 ml. of capillary blood, and compare the results with those obtained in the same subject using blood from a clean venepuncture.

A thromboplastin generation screening test was used, together with the prothrombin and proconvertin test of Owren and Aas (Scand. J. clin. Lab. Invest., 1951, 3, 201) as a test of the extrinsic coagulation system. The only possible deficiency not covered by these two tests is that of fibrinogen—a simple clotting-time estimation excludes severe degrees of hypofibrinogenaemia.

The comparisons of results from capillary and venous blood were made on a group of healthy adults and on patients with various coagulation defects. Good correlation was found between results with capillary blood and those using venous blood. It is emphasized that this method is not suitable for detailed investigation of coagulation, but that it is useful as a preoperative screening test in children.

A. Brown

532. Platelets in Blood Stored in Untreated and Siliconed Glass Bottles and Plastic Bags. I. Studies in vitro F. Kissmeyer-Nielsen. Journal of Clinical Pathology [J. clin. Path.] 14, 626-630, Nov., 1961. 2 figs., 13 refs.

The number and function (clot retraction) of platelets in blood stored at 4° C. for 3 weeks in plastic bags and in untreated and siliconed glass containers were determined using EDTA [ethylenediamine tetra-acetic acid] and acid-citrate dextrose as anticoagulants. No essential differences were found.—[Author's summary.]

533. Platelets in Blood Stored in Untreated and Siliconed Glass Bottles and Plastic Bags. II. Survival Studies F. KISSMEYER-NIELSEN and C. B. MADSEN. *Journal of Clinical Pathology [J. clin. Path.*] 14, 630-636, Nov., 1961. 6 figs., 12 refs.

Platelet survival was determined using untreated and siliconed glass bottles and plastic bags for collecting and storing blood. The platelets were tagged in vivo with P³² in 6 polycythaemic patients undergoing treatment with P³². The results showed that fresh ACD blood collected in untreated glass, siliconed glass, and plastic gave the same recovery of platelets in the recipients. The use of EDTA as anticoagulant gave results inferior to those obtained with blood using ACD as anticoagulant. Even after storage up to 24, hours in untreated glass bottles (ordinary bank blood) a satisfactory recovery of platelets was observed. After storage for 72 hours the recovery was less but not negligible.—[Authors' summary.]

534. The Partial Thromboplastin Time with Kaolin. A Simple Screening Test for First Stage Plasma Clotting Factor Deficiencies

R. R. PROCTOR and S. I. RAPAPORT: American Journal of Clinical Pathology [Amer. J. clin. Path.] 36, 212-219, Sept., 1961. 5 figs., 12 refs.

The authors of this paper from the University of Southern California Medical School, Los Angeles, describe a method of carrying out the partial thromboplastin time (PPT) test incorporating the Margolis technique of providing optimal contact activation of the test plasma by the addition of kaolin powder to the clotting mixture. The test is thereby rendered more consistent and the need for special washing of the glassware is eliminated. A method of preparing an improved partial thromboplastin is detailed.

In 40 adults the normal range of the PPT with kaolin and the improved thromboplastin was found to be 35.0 to 44.5 seconds, mean 39.5±2.0 seconds. These times are much shorter than the previously reported limits for the PPT. Studies in vitro showed that the clotting time exceeded the upper limit of normal when the calculated level of antihaemophilic globulin fell below 50%, the level of plasma thromboplastin component below 35%, the level of plasma thromboplastin antecedent below 40%, and the level of Hageman factor below 30%. The test was also carried out with plasma from patients with a variety of specific clotting factor deficiencies, the findings being similar.

This relatively simple one-stage test will not only detect a clinically significant deficiency of a plasma thromboplastic factor but will also detect the patient with mild haemophilia A or B.

A. Brown

MORBID ANATOMY AND CYTOLOGY

535. Nuclear Sexing with Aceto-orcein

A. R. SANDERSON and J. S. S. STEWART. British Medical Journal [Brit. med. J.] 2, 1065–1067, Oct. 21, 1961. 5 figs., 17 refs.

This paper from the University of St. Andrews, Queen's College, Dundee, describes the application of the aceto-orcein squash technique to the examination of oral mucosal smears for nuclear sexing. The stock stain consists of 1 g. of synthetic orcein in 45 ml. of glacial acetic acid, which is boiled, cooled, and filtered. For use 45 parts of stock are diluted with 55 parts of distilled water and filtered. Lacto-aceto-orcein consists of 50 parts of stock solution and 50 parts of 70% lactic acid, mixed and filtered. The oral mucosal smear on a clean slide is covered with a drop of stain and a cover-slip placed over it. Pressure is exerted on the preparation through filter paper to flatten the nuclei and to absorb excess stain. Simple aceto-orcein smears have to be stored covered in a refrigerator, but lacto-aceto-orcein preparations can be stored at room temperature for up to 6 weeks as the hygroscopic action of the lactic acid prevents drying. The advantage of the method is extreme speed, smears being ready for scanning with the 1/7-inch (4-mm.) oil-immersion objective at once. A

peacock blue filter (Type OB2) is recommended. A simple method of making permanent preparations is also described. Bacteria are not obtrusive in a fresh preparation, but become more deeply stained subsequently.

In a survey of 100 normal subjects all were correctly sexed by this method. In a series of 484 oligophrenic subjects 20% of smears had to be repeated because of food and bacterial contamination. Among the smears from 245 apparent males, 2 were chromatin-positive, both of these subjects being found to have the typical features of medullary dysgenesis. One of the 240 apparent females had double-positive nuclei and was apparently an example of the triple-X syndrome. Smears from the other 239 females were all chromatin-positive.

The appearance of orcein-stained cells is described and illustrated and the ease of detecting nuclear detail and sex chromatin is stressed. The findings in XXX and XXY subjects are also discussed.

F. Hillman

536. The Myenteric Plexus in Infantile Hypertrophic Pyloric Stenosis

J. R. RINTOUL and N. F. KIRKMAN. Archives of Disease of Childhood [Arch. Dis. Childh.] 36, 474-480, Oct., 1961. 11 figs., 19 refs.

The aetiology of pyloric stenosis in infants is still uncertain, but it has been suggested that the condition may be due to arrest or delay in the maturation of cells of the pyloric myenteric ganglia. In an attempt to clarify the position the authors, working in the Departments of . Anatomy of the Universities of St. Andrews and Manchester, have studied the morphological appearances of the cells of the myenteric plexus in 38 patients with congenital pyloric stenosis, from whom a wedge-shaped portion of pyloric muscle was removed at operation. Control material consisted of portions of pylorus taken from 9 newborn infants dying from unrelated causes and from 6 adults undergoing gastric surgery; two specimens each of adult duodenum and colon were also studied-Frozen tissue sections 40 μ in thickness were stained by a modified Bielschowsky-Gros silver impregnation technique and serial paraffin-embedded sections stained by Delafield's haematoxylin and eosin; some of the material was also double-embedded using 10% low viscosity nitrocellulose. Quantitative studies of the ganglion cells were not attempted.

Two distinct types of these cells were identified in the control material: (1) cells showing a marked affinity of the cytoplasm and cell processes for silver and having pale-staining nuclei, and (2) those showing little affinity of the cytoplasm and cell processes for silver and having dark-staining nuclei. Cells of Type 2 were found uniformly in the myenteric ganglia of the control material and also of the patients with pyloric stenosis, whereas Type-1 cells were almost invariably absent in the latter. In stenosed pyloric tissue no significant abnormality of the Type-2 cells could be detected when the material was stained by the silver impregnation method or other staining methods, provided the double-embedding technique was employed. When, however, the ordinary embedding in paraffin wax was used, in which there is

considerable shrinkage and often poor staining, abnormalities of the Type-2 cells were frequently seen, producing a histological picture indistinguishable from that of cell degeneration as described by Nielsen (Acta paedian. (Uppsala), 1956, 45, 636). Since similar appearances were observed in the control specimens the evidence must therefore be regarded as inconclusive. The authors suggest that the appearances described may be artefacts resulting from the inadequacies of the staining procedures employed. The lack of cells of Type 1 in pyloric stenosis may be due either to degeneration or to some developmental anomaly.

Hewett A. Ellis

537. Bronchotracheal Response in Human Influenza, Type A, Asian Strain, as Studied by Light and Electron Microscopic Examination of Bronchoscopic Biopsies

J. J. WALSH, L. F. DIETLEIN, F. N. LOW, G. E. BURCH, and W. J. MOGABGAB. Archives of Internal Medicine [Arch. intern. Med.] 108, 376–388, Sept., 1961. 10 figs., bibliography.

This is believed to be the first report on the response of the human tracheo-bronchial tree to non-fatal influenza (Type A, Asian strain) uncomplicated by bacterial infection. Of the 12 cases originally accepted for study, 3 were excluded because of the development of associated bacterial infection and 3 because of inability to establish the diagnosis by accepted laboratory methods. All but one of the 6 remaining patients were below 30 years of age; they were equally divided between the sexes and only one was a smoker.

In every case endoscopy revealed acute diffuse inflammation of the larynx, trachea, and bronchi, with mucosal injection and oedema. Microscopically, the changes varied from epithelial irregularities; such as vacuolation, oedema, and loss of cilia, to extensive desquamation. Hyperchromatic pleomorphic nuclei were seen in the epithelium, and practically all specimens showed metaplastic changes. This "pseudo-metaplasia" consistedof stratified layers of cells without cornification or flattening of the surface cells. There were no intercellular bridges. Cellular infiltrates were primarily composed of lymphocytes and histiocytes with a few plasma cells and polymorphonuclear leucocytes. There was also marked thickening and hyalinization of the basement membranes in all specimens. Electron microscopy was performed in 4 cases, and in every case revealed aggregates of particles, both intranuclear and in the cytoplasm and adjoining cytoplasmic vacuoles.

These findings are held to confirm and extend the observations of other workers made in experimental animals and in fatal cases of human influenza.

A. W. H. Foxell

538. Changes in the Hepatic Blood Vessels in Cirrhosis of the Liver

J. H. Carter, C. S. Welch, and R. E. Barron. Surgery, Gynecology and Obstetrics [Surg. Gynec. Obstet.] 113, 133-137, Aug., 1961. 3 figs., 8 refs.

A quantitative study is reported of the vasculature of 8 normal livers and 8 cirrhotic livers from patients with portal hypertension and ascites. Nécropsy speci-

mens were weighed before and after the injection of each of the 3 groups of vessels with a 12.5% solution of coloured vinyl plastic in acetone; then the corrosion cast technique of Madden et al. (Surg. Gynec. Obstet., 1954, 99, 385; Abstr. Wld Med., 1955, 17, 200) was completed by digesting the liver in concentrated HCl.

In the cirrhotic livers there was a marked reduction (by about 36% of normal) in the total vascular bed. The volume of the hepatic artery was actually increased, but that of the portal and hepatic venous trees was reduced. The marked reduction in the hepatic venous outflow (by an average of 51% of normal) is regarded as an important cause of ascites.

A. Wynn Williams

539. Morphological Aspects of Changes in the Liver in Hyperthyroldism. (Aspetti morfologici delle alterazioni epatiche nelle ipertireosi)

V. CICALA, N. FRASCOLLA, and M. RAMBALDI. Rivista di anatomia patologica e di oncologia [Riv. Anat. pat.] 19, 163–190, Feb. [received Oct.], 1961. 13 figs., 28 refs.

This paper reports a histological study, carried out at the University of Naples, of the changes occurring in the liver of patients with hyperthyroidism. Biopsy material was available for 11 cases, and necropsy material from a further 7. The biopsy specimens from the living patients showed early changes of limited extent. The hepatic cells were swollen and the cytoplasm was more acidophilic than normal. Some showed small foci of cellular necrosis and a little cellular proliferation. The normal lobular pattern was maintained, however, and the changes appeared to be reversible.

The changes in the fatal cases were much more severe; they included gross disruption of the lobular pattern, severe focal and massive necrosis of liver cells, and much hepatic cell regeneration and fibrosis. The appearances were indistinguishable from those seen in post-necrotic or portal cirrhosis. It is considered that the malnutrition secondary to hyperthyroidism is an aggravating factor in the production of this cirrhosis, but is not its cause.

H. Caplan

540. Atherosclerosis of Arterles of Neck: Postmortem Anglographic and Pathologic Study

Song Shik Choi and A. Crampton. Archives of Pathology [Arch. Path.] 72, 379–385, Oct., 1961. 5 figs., 8 refe

A simple apparatus, constructed from a blood-pressure manometer, 2 Erlenmeyer flasks, and rubber or polyethylene tubing, for injecting a suspension of finely ground barium sulphate into the carotid and vertebral arteries of cadavers is described. This permits ready radiological location of any arterial defects. The method was used in 80 consecutive necropsies on patients over 50 years of age for the detection of occlusive atherosclerotic disease. Of the 80 cases, 23 (29%) had no noteworthy radiographic abnormality in the neck arteries, 31 (39%) had mild abnormalities, 17 (21%) showed marked obstruction of at least one artery, and 9 (11%) had complete or nearly complete obstruction of at least one artery. The authors found little correlation between clinical neurological symptoms and arterial narrowing

in the neck, although when 2 neck arteries were severely narrow cerebral symptoms and lesions might be present.

A. Wynn Williams

541. Medial Necrosis of the Aorta with Secondary Arteriosclerosis in Congenital Cyanotic Heart Disease. (Aortenmedionekrose mit sekundärer Arteriosklerose bei den kongenitalen zyanotischen Herzkrankheiten)

J. L. DE FARIA. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie [Beitr. path. Anat.] 125, 129–147, Oct., 1961. 12 figs., 33 refs.

At the Faculty of Medicine of the University of São Paulo, Brazil, the ascending aorta was examined in 18 subjects aged 1 day to 17 years dying of chronic hypoxaemia due to congenital heart disease. In all cases there were necrosis and vacuolation of the muscle cells of the media, destruction of elastic fibres, proliferation of collagen fibres, and replacement of resorbed necrotic tissue with a mucoid substance. Thickening of the intima occurred, followed later by deposition of fat and the development of a typical atherosclerotic focus. These findings suggest that the primary cause of medial necrosis of the aorta is hypoxia, resulting in necrosis of the muscle cells.

M. Lubran

542. Studies on the Changes in the Aortic Endothellum with Age. (Studi sulla senescenza dell'endotelio aortico) E. FERRARI and E. FORTI. Rivista di anatomia patologica e di oncologia [Riv. Anat. pat.] 19, 146–162, Feb. [received Oct.], 1961. 9 figs., 19 refs.

Working at the Institute of Pathological Anatomy of the United Civil Hospitals, Venice, the authors have studied the endothelium of the descending thoracic aorta in subjects of various ages. Preparations stained with haematoxylin and eosin showed the normal endothelium to consist of sheets of regular elongated cells with a single nucleus and many fine granules in the cytoplasm. In the aortic endothelium of subjects who had passed the 4th decade of life collections of larger cells became apparent. These cells had plentiful cytoplasm and the nuclei were round, oval, or leaf-shaped; multinucleate forms also occurred. The changes progressed with advancing age and by the 7th and 8th decades the endothelium included many raised nodules of pleomorphic, irregular, often multinucleate giant cells, the nuclear chromatin of which was granular.

The authors are of the opinion that these changes represent a physiological reaction to mechanical stress.

H. Caplan

543. The Renal Glomerulus in Cirrhosis of the Liver W. A. Jones, D. R. Govinda Rao, and H. Braunstein. American Journal of Pathology [Amer. J. Path.] 39, 393-404, Oct., 1961. 6 figs., 29 refs.

In an attempt to decide whether a specific renal lesion did in fact accompany cirrhosis of the liver, sections of the kidney taken at necropsy in 100 patients with unequivocal cirrhosis were compared with those from 100 patients without liver disease, the sections being made by a carefully standardized technique. No differences were found in glomerular cellularity, but some thickening,

fraying, or splitting of the glomerular basement membrane was noted in 28 of the cases of cirrhosis as compared with 10 of the controls. This change was often most marked in the central portion of the glomerular tuft. Some possible causes of the lesion are discussed, but the authors, who report from the University of Cincinnati College of Medicine, Ohio, reach no firm conclusion as to its probable aetiology.

J. B. Wilson

544. Fixed and Reproducible Orthostatic Proteinurla. II. Electron Microscopy of Renal Biopsy Specimens from Five Cases

R. R. ROBINSON, C. T. ASHWORTH, S. N. GLOVER, P. J. PHILLIPPI, F. R. LECOCO, and P. R. LANGELIER. American Journal of Pathology. [Amer. J. Path.] 39, 405-417, Oct., 1961. 13 figs.; 14 refs.

'In the first part of this investigation at Lackland Air. Force Base, Texas (Amer. J. Path., 1961, 39, 291; Abstr. Wld Med., 31, 1962, 86), the authors made a lightmicroscopic study of renal biopsy specimens from cases of fixed and reproducible orthostatic proteinuria. They now report the results of examination with the electron microscope of percutaneous renal biopsy specimens from 5 cases of this syndrome. These confirmed the finding of the previous study that the increased glomerular cellularity then noted was due to collapsed or partially obliterated capillary loops, hypercellularity of glomerular loops, and increased deposits of basement-membrane substance. With the electron microscope changes in the glomerular capillary wall, with "watery" cytoplasmic swelling of its epithelium, were seen. Focal fusion of foot processes with notches representing the remains of interpedicle spaces was frequently observed. There were also changes in the cytoplasm of the swollen glomerular epithelium; the cytoplasmic bodies noted to be present were thought to be-due to an escape of protein into the glomerular filtrate.

The authors consider the basic cause of the syndrome to be a focal defect in the glomerular basement membrane permitting an increased transfer of protein.

J. B. Wilson

545. Diabetic Glomerulosclerosis: a Long-term Followup Study Based on Renal Biopsies

F. E. HATCH, M. F. WATT, N. C. KRAMER, A. E. PARRISH, and J. S. HOWE. American Journal of Medicine [Amer. J. Med.] 31, 216-230, Aug., 1961. 3 figs., 38 refs.

Sixty-four needle biopsies of the kidney were performed in '57 diabetic patients with evidence of renal disease. Forty-one patients were found to have diabetic glomerulo-sclerosis (DGS); 6 patients had other forms of renal disease. Two forms of DGS were characterized: a diffuse and a mixed (diffuse and nodular) type. There was no evidence to suggest that the mixed lesion developed from the diffuse lesion. The location of the hyaline deposits in the glomeruli remains unsettled by this study.

Clinically, proteinuria was the earliest and most persistent abnormality. A history of diabetes of more than 10 years' duration, the rare occurrence of acidosis,

and the presence of blood urea nitrogen values above 45 mg. per 100 ml. tended to suggest the mixed rather than the diffuse lesion.

The only conclusive method of making the diagnosis of DGS antemortem is by needle biopsy of the kidney. The accuracy of renal biopsy for diagnosis and follow-up was supported by the similar findings in those patients in whom autopsy was performed. The need for long-term follow-up of patients with DGS with repeated renal biopsies is stressed.—[Authors' summary.]

546. The Pathology of Asbestosis with Reference to Lung Function

B. E. Heard and R. Williams. Thorax [Thorax] 16, 264-281, Sept., 1961. 14 figs., bibliography.

This paper from the Postgraduate Medical School (Hammersmith Hospital), London, describes in detail the histology of the lesion in 6 cases of asbestosis and attempts to correlate the lesion with pulmonary function tests carried out during life. The nature of the lung lesion is discussed and attention drawn to fibrosis, which is frequently more severe in the pleura than in the pulmonary substance. This raises the question of its pathogenesis, since asbestos fibres were never found in the pleura. It is suggested that a hypersensitivity mechanism, such as has been postulated in silicosis, may also apply in asbestosis. The associated presence of emphysema and bronchiectasis was also noted. The correlation between pathological lesions and clinical tests was good. though the explanation of deficient function was not always clear. It was not possible to decide whether the reduced inspiratory capacity and decreased lung volume were due to the more prominent pleural adhesions or to pulmonary shrinkage and fibrosis. Reduction in diffusing capacity might have been due to a decrease in the total area of alveolar membrane or to a reduction in the permeability of the membrane per unit area. The association with cancer described by other workers was con-

[This paper is beautifully illustrated, and its worth can only be appreciated by reading it in full.]

G. J. Cunningham

547. The Ling Lining Film in Some Pathological Conditions

R. E. PATTLE and F. BURGESS. Journal of Pathology and Bacteriology [J. Path. Bact.] 82, 315-331, 1961. 20 refs.

The normal lung alveoli are lined with a surface film of lipoprotein. The properties of this film have been deduced by observing the behaviour of bubbles which have been squeezed out of ling tissue into air-saturated water. The lipoprotein film lowers the surface tension of the bubble and thus gives it a certain degree of stability, and the state of the lining film can be assessed by measuring the "stability ratio" of such bubbles, which is the relation between the final stable surface area and the initial surface area. The work reported in the present paper from the Chemical Defence Experimental Establishment, Porton Down, Salisbury, has been carried out on experimental animals and a stability ratio for normal lungs calculated. As post-mortem autolysis and chemi-

cal fixatives interfere with the formation of this lipoprotein film on bubbles, only fresh material can be used for such investigations.

Pathological conditions were induced by the infratracheal injection or inhalation of toxic substances such as phosgene, cadmium oxide, lysolecithin, and "tween 80". Non-toxic lesions were produced by simple collapse following bronchial obstruction and blast damage, and by other devices. It was found that ability to form a lining film on bubbles as indicated by a normal stability ratio was frequently related to the behaviour of the lung after inflation had been released. Those lungs yielding bubbles of normal stability ratio remained aerated, while those giving bubbles with a low stability ratio tended to collapse. The study of pathological lesions showed that in many cases the power of formation of the lining film was not impaired. If, however, the toxic agent employed was a surface-acting material such as lysolecithin or tween 80, then production of the surface film was impaired, as revealed by a lowered stability ratio of the bubbles.

[While these findings are of the greatest interest the actual cause of failure to form a lining film is as yet obscure and awaits further research.]

G. J. Cunningham

548. The Formation of a Lining Film by Foetal Lungs.

R. E. PATTLE: Journal of Pathology and Bacteriology [J. Path. Bact.] 82, 333–343, 1961. 19 refs.

The existence of a lipoprotein living film of normal lung helps to maintain the patency of the alveoli. It was thought that failure to form such a film might play a part in the development of hyaline membrane disease in human infants.

A study was therefore made of foetal lungs of rats, mice, and guinea-pigs. It was found that all lungs which had become inflated spontaneously possessed the power of forming a lining film. Less mature lungs frequently failed to do so. The power to form a lining film was correlated with the stages in histological development—that is, when desquamation of the cuboidal epithelium from the larger lumina is almost complete a lining film resembling that of adult lung could be formed. It is suggested that surface-acting agents derived either from decomposition of the lung lining or from the amniotic fluid might inhibit the formation of a lining film and so play a part in the causation of hyaline membrane disease:

[This article must be read in conjunction with the previous article by Pattle and Burgess (see Abstract 547).]

549. Neuropathological Observations in Maple Syrup Urine Disease: Branched-chain Ketoaciduria

J. SILBERMAN, J. DANCIS, and I. FEIGIN. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 351-363, Oct., 1961. 11 figs., 19 refs.

"Maple syrup" disease, or progressive familial infantile cerebral dysfunction, was first reported by Menkes et al. (Pediatrics, 1954, 14, 462) and owes its name to the characteristic maple-syrup-like odour of the patient's urine. It is believed to be another of the diseases due to

"an inborn error of metabolism", and is invariably fatal. In this report from New York University School of Medicine and Bellevue Hospital, New York, the authors describe the pathological changes in the brains of 4 infants who died of the disease at the ages of 9, 91, 13, and 20 months respectively.

In the first case the central white matter of the cerebellum appeared grey and granular around the dentate nuclei. In the second case 2 areas similar in appearance were present in the parieto-occipital white matter. Of the other 2 cases the brain in one appeared to be normal, while in the other there was cerebral oedema, but no other relevant abnormalities. The histological changes consisted in deficient myelination, status spongiosus, a decrease in the number of oligodendroglia, and astrocytosis. No products of myelin breakdown were found except in the second case, in which phagocytes containing lipid were present in the perivascular spaces. Perivascular inflammatory cells were present in the first and fourth cases.

The intensity of defective invelination decreased with the age of the patient. The pattern of myelination was different from that occurring in normal infants at an earlier age, and focal areas of myelin deficiency were found around the dentate nuclei in Case 1. The axons were relatively normal apart from slight focal irregularities. Astrocytosis tended to be proportional to the myelin deficiency. Attention is drawn to the similarities of the histological findings in the present cases to those in cases of infantile spongy degeneration described by Canavan (Arch. Neurol. Psychiat., 1931, 25, 299) and by Van Bogaert and Bertrand (Acta neurol. belg., 1949, 49, 572), and also in cases of phenylpyruvic oligophrenia.

H. S. Schutta

550. An Electron Microscopic Study of Eccrine Sweat Glands in Patients with Cystic Fibrosis of the Pancreas B. L. Munger, S. W. Brusnow, and R. E. Cooke. Journal of Pediatrics [J. Pediat.] 59, 497-511, Oct., 1961. 12 figs., 39 refs.

The morphology of the eccrine sweat glands in cystic fibrosis of the pancreas was studied by electron microscopy in 8 patients, aged 11 months to 8 years, at Johns Hopkins Hospital, Baltimore. With a high-speed punch instrument skin biopsy specimens were obtained from the volar aspect of the forearm before and after pilocarpine stimulation in 6 of the patients and in the resting state in 2. The tissue was placed in Dalton's chromeosmium fixative and embedded in methacrylate, sections being examined by phase, light, and electron microscopy. The gallocyanin chrome alum stain for basophilia, a modified Hale colloidal iron stain for acid mucopolysaccharides, and the periodic acid-Schiff method for glycogen were additional aids for light microscopy. By routine light and phase microscopy the eccrine sweat glands appeared to be normal. Mucoid cells, however, were less basophilic than normal and contained fewer secretory vacuoles before and after pilocarpine, stimulation. By electron microscopy the vacuoles were seen to have a normal content, but unidentified small dense bodies were-present in all the secretory cells in numbers A. Wynn Williams greater than normal.

Microbiology and Parasitology

551. Human-amnion-tissue Culture in the Routine Virus

I. B. R. DUNCAN and E. J. BELL. British Medical Journal [Brit. med. J.] 2, 863-866, Sept. 30, 1961. 6 refs.

The authors, working at the University Virus Laboratory. Glasgow, have compared the susceptibility to enteroviruses of cultures of human amnion cells and of monkey kidney cells. Titrations of a wide range of enteroviruses in both types of cell culture gave similar results in most cases, except that no cytopathic effect was observed in amnion cells infected with Coxsackie viruses B2 and B4 or E.C.H.O. viruses Types 4, 10, 14, 16, and 27. During the course of one year amnion cells were used to isolate virus from stool specimens from which virus had already been isolated in monkey kidney cells; virus was demonstrated in most specimens except those infected with Coxsackie-B viruses. Virus was also isolated in amnion cells from 13 out of 19 cases of herpes simplex, whereas it was obtained from only 10 of the cases by inoculation of chick chorio-allantoic membrane.

On average 460 tubes were obtained from one amnion; successful culture appeared to depend on the viability of the amnion cells at the time of delivery rather than on subsequent handling in the laboratory. The authors recommend this economical and readily accessible source of tissue culture material for use in the virus laboratory not having access to monkeys, and suggest that the failure to isolate Coxsackie-B viruses in human amnion tissue can be remedied by using suckling mice when indicated.

Janice Taverne

552. Isolation of Syncytlal Virus (C.C.A. Virus of Morris) during Epidemic Benign Respiratory Illnesses in Premature Infants. (Isolement du virus syncytial (virus C.C.A. de Morris) au cours de manifestations, respiratoires bénignes épidémiques chez des prématurés)

A. Breton, J. Samaille, B. Gaudier, —. Gerard-Lefebure, and C. Ponté. Archives françaises de pédiàtrie [Arch. franç. Pédiat.] 18, 459-467, April [received Nov.], 1961. 5 figs., 6 refs.

Early in 1960 at the Premature Infant Centre of the Clinique Médicale Infantile, Lille, 12 babies aged 1 to 3 months acquired an infection of the upper respiratory tract. Although they had no increase of temperature, they all developed a dry cough, rhinitis, and coryza, which cleared up in about a week. Radiological changes corresponding to those commonly described in bronchopneumonia caused by viruses were observed in 8 of the 12 infants. A virus was isolated directly in KB cells from 2 of the cases and neutralizing antibodies to the virus appeared in serum from 5 of them. The virus caused the formation of syncytia in KB and HeLa cell cultures, but it did not grow in eggs or in laboratory animals and it did not cause haemagglutination. It was extremely labile, being rapidly inactivated at room temperature and at -20° C., and its infectivity was destroyed

by ether. Cross-neutralization tests showed it to be identical with the C.C.A. (chimpanzee coryza agent) virus first described by Morris et al. (Proc. Soc. exp. Biol. (N.Y.), 1956, 92, 544) and isolated from human cases by Chanock et al. (Amer. J. Hyg., 1957, 66, 281 and 291; Abstr. Wld Med., 1958, 24, 87).

Janice Taverne

553. Studies on Staphylococci of Phage Type "80/81" G. WALLMARK and M. FINLAND. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 279-285, Sept., 1961. 14 refs.

The investigation herein reported from the City Hospital and Harvard Medical School, Boston, was directed towards determining: (1) whether certain phage types of staphylococci commonly employed, in this instance Types 52 and 42B, had mutated since their original isolation and had acquired a different host range from the original set, and (2) whether the Type 80/81 might be separated into distinct types or whether it was a single unit. A standard typing technique was employed; tests for lysogenicity were carried out by the cross-culture method of Fisk, and the susceptibility of the strains to antibiotics was also determined. It was found that: (1) there had been an alteration in the specificity of phages of Types 52 and 42B, so that variants of these phages now lysed strains previously typed as 80/81/KS6; (2) there were 9 different patterns within the group designated "80/81" (the phages employed were 80, 81, KS6, 52, 52A); and (3) the antibiotic sensitivity pattern of the group 80/81 was variable, the majority of strains being resistant to penicillin, streptomycin, and tetracycline, and about a quarter to erythromycin.

The value of recording the sensitivity pattern for epidemiological purposes is discussed. John M. Talbot

554. Investigations on Influenza Virus and Influenza Vaccines. (Untersuchungen über das Influenza-Virus und Influenza-Impistoffe)

J. Potel and S. Hlawatsch. Zeitschrift für Immunitätsforschung und experimentelle Therapie [Z. Immun.-Forsch.] 122, 58–78, Sept., 1961. 9 figs., 48 refs.

The authors have shown that inactivation of influenza virus by 0.05% formalin at 4° C. or its exposure to temperatures of 20° and 37° C. reduces considerably its infectivity, its haemagglutination power, and its antigenicity. Such reduction is much less with 0.5% phenol or 1:1,000,000 thiocide. The antigenicity of the virus can be greatly increased by adsorption on to alumina, as judged by antibody production in guinea-pigs and mouse-protection tests. In human subjects given a single subcutaneous dose of alumina-adsorbed virus of Types A and A2 there were increased antibody levels and higher haemagglutination titres, and these were maintained for at least 12 months. Little augmentation resulted from a second injection after about a year.

M. Lubran

555. The Effect of Tolbutamide on Human Basal Gastric

A. WEISS and W. J. SCIALES. Annals of Internal Medicine [Ann. intern. Med.] 55, 406-415, Sept., 1961. 3 figs., 22 refs.

The authors report the results of a study of the effectof the antidiabetic agent tolbutamide on gastric secretory. function, carried out at Flushing Hospital and Dispensary, New York. Taking part in the investigation were 21 patients not suffering from diabetes mellitus or organic disease of the gastro-intestinal tract. Basal gastric secretion was estimated by continuous suction of gastric con-- tents via a Levin tube sited radiologically in the gastric antrum, and further studies were made after the intravenous injection of 1 g. of tolbutamide. It was found that there was a significant increase in basal gastric secretion in respect of volume, of pepsin output, and of free and total acid output in 15 (71.4%) of the group. The rise and subsequent fall in basal gastric/secretion was found to correlate with the hypoglycaemic response to tolbutamide, and thus the authors consider there is no evidence that tolbutamide has a direct stimulating effect on gastric secretion; consequently any stimulating effect is mediated via hypoglycaemia and the central vagal pathway. This effect would seem to be rarely important A. E. Read enough to produce clinical aggravation of peptic ulcers in diabetic patients.

556. Circulatory Effects of Guanethidine in Hypertensive Heart Failure

Nº 16 4

S. B. Roy, V. S. MATHUR, and M. L. BHATIA. Medical Journal [Brit. med. J.] 2, 1315-1317, Nov. 18, 1961. 2 figs., 10 refs.

A study of the haemodynamic effects of guanethidine in hypertensive patients in heart failure is reported from the All India Institute of Medical Science, New Delhi. Cardiac catheterization was carried out on 7 patients, all of whom had a raised venous pressure and other evidence of heart failure. Data on cardiac output and systemic and pulmonary blood pressures were obtained before and 30 minutes after rapid administration of 10 to 20 mg, of guanethidine into the pulmonary artery.

In the majority of the patients the authors observed under these conditions a fall in right atrial pressure and right ventricular end-diastolic pressure, an increase in cardiac output, and a fall in both pulmonary and systemic arterial pressures and in the calculated peripheral resistance. The heart rate also slowed in most patients. In 2 patients there was no change in systemic arterial pressure and also no change in cardiac output. [No mention is made of any rise in arterial pressure immediately following guanethidine given by this route, as reported by other workers; this has been thought to be a possible. danger of intravenous administration of the drug in patients with heart failure.]

A total of 11 patients with hypertensive heart failure. including the 7 studied in detail, were given guanethidine by mouth for an average period of 4 months. One patient died from cardiac infarction, but the others responded well, only 3 needing diuretics and one diuretics and digitalis in addition. The authors conclude that guanethidine is a useful drug in the management of hypertensive heart failure. M. Harington '

557. Pharmacological Studies with Polythiazide, a New Diuretic and Antihypertensive Agent

A. SCRIABINE, B. KÖROL, B. KONDRATAS, M. YU, S. Y P'AN, and J. A. Schneider. Proceedings of the Society, for Experimental Biology and Medicine [Proc. Soc. exp. Biol. (N.Y.)] 107, 864-872, Aug.-Sept. [received Nov.], 1961. 5 figs., 20 refs.

In experiments at the Pfizer Research Laboratories, Groton, Connecticut, the diuretic and antihypertensive effects of polythiazide (2-methyl-3- $(\beta, \beta, \beta$ -tri-fluoroethylthiomethyl)-6-chloro-7-sulphamyl-3:4-dihydro-1:2:4 benzothiodiazine 1:1-dioxide) were compared with those of chlorothiazide, benzthiazide, and trichlormethiazide in rats and dogs. When given orally to rats polythiazide was shown to be 2.9, 9.9, 5.5, and 0.4 times more potent than trichlormethiazide in increasing urinary volume and urinary excretion of sodium, chloride, and potassium respectively. It was 40 times as potent as benzthiazide and 400 to 600 times more potent than chlorothiazide in its natriuretic and chloruretic effects. In dogs polythiazide produced an increase in sodium and chloride excretion in animals given a water load, the effect being apparent within 20 minutes of the intravenous injection of the drug and within one hour when polythiazide wasgiven orally; 'also the duration of its action was greater than that of trichlormethiazide. Further, polythiazide did not affect the urinary pH, the excretion of bicarbonate and ammonium ions, or the glomerular filtration

In experimental acidosis polythiazide increased sodium excretion, slightly increased potassium excretion, and slightly reduced urinary pH and bicarbonate excretion. In alkalosis the drug had the usual effects on sodium. potassium, and chloride excretion, but produced a considerable increase in bicarbonate excretion. Tests in vitro showed that polythiazide produced a 50% inhibition of carbonic anhydrase at a concentration of 5×10^{-7} M. In hypertensive dogs polythiazide in an oral dosage of 400 µg. per kg. body weight per day caused a decrease in blood pressure which was maximum on the 5th day of treatment. Blood pressure was lowered in hypertensive rats on the 2nd or 3rd day of treatment with 100 μ g. per day. However, doses of 1 to 50 mg. of polythiazide per kg. given intravenously to normotensive anaesthetized dogs was without effect on the blood pressure, but they P. A. Nasmyth were only observed for 4 hours.

558. The Gastrointestinal Absorption of Oral Iron-Dextran and Ferrous Sulfate

P. A. RAGEN, L. WALKER, G. D. SPARLING, and R. P. PILLOW. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 454-456, Oct., 1961. 3 refs.

In a study at the Mason-Clinic, Seattle, Washington, to compare the gastro-intestinal absorption of iron 8 apparently healthy subjects received by mouth a dose of ferrous sulphate solution containing enough 59Fè to give $1\,\mu\text{c}$. of radioactivity and, 14 days later, a dose of iron-dextran complex to give the same degree of radioactivity. The radioactivity of the subsequent stools was determined and iron absorption calculated from the difference between intake and excretion. This absorption amounted to an average of 52% for ferrous sulphate and 51% for the iron-dextran complex. Since, however, the latter contained 354 μg : of elemental iron as against 50 μg . in the ferrous sulphate solution, the iron absorbed from the iron-dextran complex averaged 180 μg : as against 26 μg for the ferrous sulphate.

V. J. Woollev

559. Effect of Anticoagulant Therapy upon Aspirininduced Gastrointestinal Bleeding
R. M. WATSON and R. N. PIERSON JR. Circulation

[Circulation] 24, 613–616, Sept., 1961. 2 figs., 18 refs.

In an investigation at St. Luke's Hospital, New York, to evaluate the safety of salicylate ingestion in combination with anticoagulant drugs 25 patients who were 'receiving nicoumalone ("sinthrome") orally to preventcomplications of coronary arterial disease, thrombophlebitis, and auricular fibrillation were studied for évidence of gastro-intestinal loss of blood during a control period and during a period of aspirin administration (600 mg. 4 times daily). The average daily loss of blood during the control period was 0.1 to 3.2 ml., and during the period of aspirin administration 0.8 to 13.0 ml., compared with 0 to 1.9 ml. and 0.5 to 85 ml. respectively for a control group of healthy volunteers. The majority of patients required reduction in the dosage of nicoumalone during aspirin administration, indicating decrease in prothrombin activity. I. Ansèll

560. Effects of Steroid-17-spirolactones on Aldosterone Secretion, Excretion, and Metabolism in Man

E. T. DAVIDSON, W. S. COPPAGE JR., D. ISLAND, and G. W. LIDDLE. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 505-514, Oct., 1961. 4 figs., 18 refs.

In a study undertaken at the Vanderbilt University School of Medicine, Nashvillé, Tennessee, to determine whether the spirolactones directly influence the adrenal secretion of aldosterone 5 normal control subjects, one patient with primary aldosteronism, one with nephrosis, and one with hepatic cirrhosis, all being kept on a fixed daily electrolyte intake, were given spirolactones or ally or intramuscularly in a dosage of 400 to 750 mg. daily in divided doses for 3 to 6 days; in 2 studies 50 μ g. (20 μ c.) of tritum-labelled aldosterone was given intravenously in order to determine the aldosterone excretion rates. Samples of 24-hour collections of urine were

analysed for radioactive aldosterone, "tetrahydroaldosterone", 17-hydroxycorticoid, 17-ketosteroid, and sodium and potassium content.

The urinary excretion of sodium and chloride was increased and that of potassium and ammonia decreased in all the subjects with intact adrenal glands. The excretion of radioactive aldosterone and tetrahydroaldosterone was either unchanged or increased. The aldosterone excretion rate, estimated by determining the degree of dilution of labelled aldosterone in the urine over a given time, was unchanged. No consistent alteration in 17-hydroxycorticoid or 17-ketosteroid, excretion was observed to result from the administration of a spirolactore.

The authors conclude that the spirolactones act by reversing the effect of aldosterone on electrolyte excretion in the renal tubules, probably by competitive inhibition, and do not directly influence aldosterone excretion, metabolism, or excretion by the kidneys. The increase in urinary aldosterone excretion which may follow spirolactone therapy is attributed to loss of total body sodium, which is in itself the physiological stimulus for increased aldosterone secretion by the adrenal glands.

Gerald Sandier

561. The Effect of Dosage Form upon the Gastrointestinal Absorption Rate of Salicylates

G. LEVY, R. H. GUMTOW, and J. M. RUTOWSKI. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 414-419, Aug. 19, 1961. 4 figs., 17 refs.

In a survey of the effect of dose level on the absorption rate of salicylates by the gastro-intestinal tract, carried out at the University of Buffalo School of Pharmacy, New York, 12 healthy males aged 19 to 27 years and weighing 155 to 190 lb. (70 to 86 kg.) received on separate occasions, on an empty stomach, 10 gr. (650 mg.) each of 2 brands of plain aspirin tablets, aspirin tablets combined with aluminium glycinate and magnesium carbonate, an aqueous solution of sodium salicylate, and a solution of choline salicylate. Salicylate in the urine was determined colorimetrically one hour after ingestion and 2-hourly thereafter up to 9 hours.

The subjects who had had aspirin solution excreted an average of 4 to 6 mg. of salicylate after the first hour, which increased rapidly at the 3rd hour to an average of 95 to 99 mg., reaching an average of 265 to 283 mg. at the 9th hour. The subjects who had had aspirin tablets excreted 12.5 to 17.2 mg. after the first hour, the level again rising rapidly after the 3rd hour to average 83 to 87 mg, and reaching 252 to 274 mg, after the 9th hour. The authors compare statistically the excretion after one hour of the various salicylate solutions with that of aspirin tablets, and find that the 2 brands of tablet vielded significantly lower salicylate absorption rates than. choline salicylate solution. One brand of aspirin tablet was more rapidly absorbed than the other, but there was no difference in absorption between the 3 aspirin solutions. The absorption appears to be not so much; affected by the type of aspirin used as by its vehicle of administration.

The authors conclude that there are significant differences in dissolution rate of different brands of aspirin

tablet, and the rate at which these tablets dissolve is the rate-controlling process in aspirin absorption. To obtain rapid drug absorption and to reduce contact irritation in the stomach aspirin solutions prepared with small amounts of alkaline compounds may be used.

Anne Tothill

562. Differential Effects of Phenobarbital, Pentobarbital and Diphenylhydantoin on Motor Cortical and Reticular Thresholds in the Rhesus Monkey. [In English]
R. Aston and E. F. Domino. Psychopharmacologia

R. Astron and E. F. Domino. *Psychopharmacologia* [*Psychopharmacologia* (*Berlin*)] 2, 304–317, 1961. 5 figs., 19 refs.

The clinical use of phenobarbitone and diphenyl-hydantoin in epilepsy derives from earlier experimental work by various authors who showed that these drugs diminish the motor cortical response to stimuli. In this study, carried out at the University of Michigan, Ann Arbor, to re-examine the experimental basis for the medication of epilepsy bipolar electrodes were implanted permanently in the motor cortex, the mesencephalic reticular system, and the anterior hippocampal areas of rhesus monkeys, in which stimuli necessary to produce motor seizures and alerting responses were then determined before and after various doses of pentobarbitone, phenobarbitone, and diphenylhydantoin.

It was found that diphenylhydantoin was the most specific of the 3 drugs in increasing the motor cortical threshold while not affecting the reticular threshold. Phenobarbitone raised the motor cortical threshold and slightly raised the reticular threshold, while pentobarbitone increased both the motor and reticular thresholds. The anaesthetic potency of the drugs was shown to be correlated with their effects upon the reticular threshold.

[The full details of this study cannot be given in an abstract, but they provide data that explain the usefulness of phenobarbitone and diphenylhydantoin in certain types of epilepsy.]

B. M. Davies

563. Electromyographic Method for Objective Measurement of Muscle Relaxant Drugs

C. R. Peterson and C. S. Wise. Archives of Physical Medicine and Rehabilitation [Arch. phys. Med.] 42, 566-572, Aug., 1961. 7 figs., 9 refs.

In this study the authors, working at the George Washington University School of Medicine, Washington. D.C., have evaluated the effects of "carisoprodol" as a muscle relaxant in patients with upper motor neurone spasticity by measuring electromyographically a controlled patellar reflex. In all, 30 experiments were per-"formed on 23 subjects, of whom 20 had disseminated (multiple) sclerosis with spastic lower extremities and 3 had spastic hemiplegia secondary to cerebral vascular accidents. The patient being tested was strapped in a knee brace with the knee flexed to approximately 30 degrees, motion of the knee being prevented. Quadriceps muscle electrical activity was recorded by surface electrodes connected to an electromyograph, and a weighted patellar hammer was attached to the brace in such a way that a standard-controlled stimulus could be applied. The action potentials produced were recorded photo-

graphically. In each case three control readings were taken at 15-minute intervals before administration of the drug or the placebo, and further readings recorded 30, 60, 90, and 120 minutes after its administration; in 61 tests the patients were given 800 mg. of carisoprodol, in 13 they received 1,200 mg., and in 11 studies the placebo was given.

The results indicated that the depression of the quadriceps action potential in the patients receiving the drug was statistically significant. The authors point out that this does not enable conclusions to be drawn regarding the clinical effectiveness of the drug, for which clinical trials are necessary. They do suggest, however, that the technique described appears to be applicable to the screening and objective comparative evaluation of neurospasmolytic agents.

Renneth Tyler

564. Drug-induced Extrapyramidal Reactions. Treatment with Diphenhydramine Hydrochloride and Dihydroxyphenylalanine

P. L. McGeer, J. E. Boulding, W. C. Gibson, and R. G. Foulkes. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 665-670, Sept. 9, 1961. 18 refs.

Ataractic drugs such as phenothiazine and derivatives of rauwolfia frequently give rise to extrapyramidal signs and symptoms, the typical picture in a severe case being that of drug-induced Parkinsonism. Withdrawal of the offending drug usually results in disappearance of the extrapyramidal reaction within a few days, but sometimes reduction in dosage or transfer of the patient to another tranquillizing drug is sufficient. The reaction can often be corrected by the administration of specific anti-Parkinsonian agents, which may be either anticholinergic : or antihistaminic, or both. In this paper from the University of British Columbia, Vancouver, the authors describe a study, carried out on female patients in a mental hospital, which was designed to test the theory that the normal functioning of the extrapyramidal system depends upon a balance between two competing systems of neurohormones, namely, the acetylcholine-histamine system and the catecholamines-serotonin system, since it has been suggested that drugs producing extrapyramidal reactions do so because of an interference with the catecholamines-serotonin system. They therefore compared the effects of two drugs, dihydroxyphenylalanine (DOPA) and diphenhydramine, in the treatment of these extrapyramidal reactions, DOPA being given to correct the balance in favour of the catecholamine-containing system, whereas diphenhydramine was intended to do so ... by interfering with the histamine-containing system.

Of 22 patients given DOPA in doses of 4 to 32 g. daily, only 4 were mildly benefited. In contrast, in all of 11 patients treated with diphenlydramine, in doses of 0.4 to 0.6 g. daily, the extrapyramidal reactions were well controlled. Thus the antihistamine was clearly more effective than the catecholamine precursor. In the patients given diphenhydramine the extrapyramidal reactions were quickly controlled and there was noticeable improvement by the following day; whereas in those given DOPA the results were poor, despite therapy for 3 to 7 days.

P. T. Main

Chemotherapy

565 (a). Chemotherapeutic Studies on a New Antifungal Agent, X-5079C, Effective against Systemic Mycoses E. Grunberg, J. Berger, and E. Titsworth. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 504-506, Oct., 1961. 4 refs.

565 (b). Chemotherapeutic and Toxic Activity of the Antifungal Agent X-5079C in Experimental Mycoses

C. W. EMMONS. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 507-513, Oct., 1961. 6 refs.

565 (c). Chemotherapeutic Activity of X-5079C in Systemic Mycoses of Man

J. P. UTZ, V. T. ANDRIOLE, and C. W. EMMONS. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84,514-528, Oct., 1961. 2 figs., 6 refs.

These three papers deal with a new antifungal agent, X-5079C, which is a polypeptide derived from streptomyces. The first paper, from a pharmaceutical research laboratory, reports that the agent is active in vitro against Histoplasma capsulatum and Blastomyces dermatitidis, but has no effect against pathogenic bacteria, the dermatophytes, or Candida albicans. It was also shown to be active against experimental infection of mice with H. capsulatum or B. dermatitidis, but not against infections with pathogenic bacteria, protozoa, or viruses, or against. transplanted tumours. The author of the second report, from the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, was not impressed with the action of the drug in vitro against H. capsulatum, Candida neoformans or C. albicans. However, it did prevent death in mice experimentally infected with Histoplasma, and was partly effective in blastomycosis and coccidioidomycosis; but ineffective in cryptococcosis. Acute toxicity studies in mice showed a 1,200-fold difference between the lethal dose and the effective therapeutic dose, which, as the author points out, is a remarkable margin of safety.

The third paper, from the same Institute as the second, describes a clinical study of X-5079C and reports the results of treatment in 28 cases of severe systemic mycoses. The drug was given subcutaneously every 6 hours in a dose of 3 to 17 mg. per kg. body weight per day (usually 4 mg. per.kg.) for up to 10 weeks (mean 4 weeks). Of 8 patients with histoplasmosis, 3 recovered, 3 were improved, and 2 were unchanged, while of 6 patients with blastomycosis, 5 recovered and the sixth was remarkably improved. Two patients with aspergillosis (pulmonary in one and disseminated in the other) and 3 with sporotrichosis involving the bones and joints were also improved, and one patient with maduromycosis recovered. It is noted that many of these cases had failed to respond to treatment with the stilbamidine type of drug or with amphotericin, hitherto the most effective known remedies for the systemic mycoses: On the other hand, of 6 cases of coccidioidomycosis, 5 failed to respond and the 6th was treated for only a short time; also 2 patients with

Candida endocarditis died in spite of therapy. It is thought that these two infections may be less responsive to the drug.

[Specific treatment for the systemic fungal infections has hitherto been disappointing, but the above reports on this new antifungal agent appear to hold out great promise of more effective therapy in the future.]

T. B. Begg

566. Experimental and Clinical Experience with a New Sulphonamide in Paediatric Practice. (Experimentelle und klinische Erfahrungen mit einem neuen Sulfonamid in der Kinderheilkunde)

H. SCHÖNFELD and S. SEIDL. Chemotherapia [Chemotherapia (Basel)] 3, 25=34, 1961. 3 figs., 34 refs.

The authors report from the City Children's Hospital, Berlin-Wedding, their experience with a new longacting sulphonamide known as "methoxin" or "kiron" and having the chemical structure 3-sulphanilamido-5methoxy pyrimidine. Toxicity studies showed that the LD₅₀ for rats was 1.2 g. per kg. body weight when given intravenously and 4 g. per kg. when given by mouth. Solubility of the free compound is 18.0 mg. per 100 ml. at pH 5 and 184 mg. per 100 ml. at pH 8. The concentration of the drug in the blood was estimated by the method of Bratton and Marshall (J. blol. Chem., 1939, 128, 537) in 2 ml. of whole blood from 6 infants who had received an oral dose of 40 mg. per kg. body weight. This showed that the maximum concentration of free sulphonamide occurred after 5 hours, when it was 12·1 mg. per 100 ml., falling to 1.23 mg. per 100 ml. after 72 hours. Acetylation in the blood was of the order of .14.5%. Even after 8 days of the recommended maintenance dosage of 20 mg, per kg, body weight there was no excessive accumulation of the drug in the blood, the level being 2 mg. per 100 ml. at the end of 7 days. Tests carried out on 3 infants showed that 50% of the amount in the urine was acetylated, thus decreasing the danger of crystallization in the urinary tract.

In the clinical trial 56 infants with pneumonia, upper-respiratory tract infections, otitis, tonsillitis, and pyuria were treated with the drug. The initial dose was 40 mg. per kg. body weight, reduced on the second day to 20 mg. per kg. and continued for 4 to 12 days. The drug, dissolved in tea, was well taken by all the patients. There were no toxic effects and, despite the low urinary solubility, no sedimentation in the urine. Uniformly good results were obtained in cases of otitis, catarrhal infections, and bronchopneumonia, although in this last condition parallel radiological recovery did not occur until later. One case of enterococcal pyuria was not benefited by methoxin, but the condition cleared after a course of chloramphenicol.

In spite of the relatively small number of cases treated, the authors consider that the drug shows promise, but agree that fuller studies will be necessary for its accurate appraisal.

I. M. Librach

CHEMOTHERAPY OF TUMOURS

567. Clinical Experience with Vinblastine Sulfate O. H. WARWICK, R. F. ALISON, and J. M. M. DARTE. Canadian Medical Association Journal [Canad. med. Ass.] J.] 85, 579-583, Sept. 2, 1961. 1 fig., 13 refs.

This clinical trial of the effect of vinblastine sulphate (vincalcukoblastine) on malignancy was carried out at the Ontario Cancer Institute and the Princess Margaret. Hospital; Toronto, on 120 patients, of whom 31 had Hodgkin's disease, 15 lymphoma, 20 leukaemia, 9 testicular tumours, and 4 choriocarcinoma, the other 41. having miscellaneous solid tumours. In all cases the patients had received previous treatment, which had failed; during the present trial only 4 of the patients with Hodgkin's disease received additional therapy, in the form of radiation, and these are not included in the analysis of results. All the patients were given vinblastine sulphate in a dosage of 0.2 mg, per kg, body weight, administered in 10 divided doses at hourly or half-hourly intervals into the tubing of an intravenous infusion of 5% glucose in normal saline. This dose was repeated 7 to 10 days later if the leucocyte count had not fallen below 3,000 per c.mm. Treatment was discontinued if no response was observed.

In fact 84 of the patients showed no response. Of the remaining 32, 16 who had advanced Hodgkin's disease showed marked improvement, which lasted 2 weeks to 11 months. In 4 patients with acute stem-cell leukaemia there was some alleviation of symptoms and signs lasting 4 to 8 weeks. In one case each of carcinoma of the breast, carcinoma of the stomach, leukosarcoma, réticucum-cell sarcoma, plasma-cell myeloma, unspecified lymphoma, giant follicle lymphoma, choriocarcinoma, seminoma, and teratoma of the testis remissions occurred, but 2 cases of lymphosarcoma showed only short remissions.

Few-serious toxic effects were seen, 73 of the patients suffering no adverse effects other than leucopenia. Local irritation, pain, thrombophlebitis, and nausea orfever occurred in 20 patients, while 2 patients developed temporary partial alopecia, 2 hyperuricaemia, and 2 hyperuricuria.

The authors discuss separately a group of 6 patients with advanced Hodgkin's disease, in 4 of whom the disease remitted but the other 2 died. They conclude that vinblastine sulphate is useful in the treatment of Hodgkin's disease, particularly when the patient is resistant to alkylating agents, but should be reserved for advanced cases only, localized Hodgkin's disease being best treated by radiotherapy. Anne Tothill

568. Vincaleukoblastine in the Treatment of Malignant Disease

D. M. WHITELAW and J. M. TEASDALE. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 584-591, Sept. 2, 1961. 4 figs., 6 refs.

From the University of British Columbia, Vancouver, the authors report an investigation into the cytotoxic properties of vincaleukoblastine, an alkaloid obtained , 1086-1099, Oct., 1961. 10 figs., bibliography.

from the Madagascar periwinkle, which was carried out on 42 male and 13 female patients aged from 14-to 78 years, of whom 37 had previously received other forms. of treatment; 24 of the 55 patients were in a poor or terminal state, when treatment with vincaleukoblastine. was started. The first 6 patients received the drug in a dosage of 0.15 mg, per kg, body weight intravenously daily for 3 or 4 successive days. As this dosage produced profound effects on the bone marrow and in some patients severe generalized toxicity manifested by weakness, rising fever, and anorexia, which hastened death, the remainder were treated with doses of 10 mg, given intravenously at intervals of 3 or 4 days or longer, depending on the response of the disease and the reaction of the bone marrow. Children received a dosage of 0.15 mg. per kg, at the same intervals as the adults. In doses of this order the drug was well tolerated by the majority of patients, but in several cases maintained on toxic weekly doses malaise occurred 24 hours after the injection and lasted for 12 hours. Anorexia, nausea, and vomiting were the commonest symptoms noted but were always transient. The substance was irritant when injected subcutaneously.

Vincaleukoblastine caused a fall in the leucocyte count to below 4,000 per c.mm. in all non-leukaemic patients, the count falling to below 2,000 per c.mm. in some twothirds of them. Recovery from leucopenia started within 14 days of discontinuing the drug. Platelet counts were unaffected in 32 patients, but in 5 the count was considerably reduced. A fall in the reticulocyte count and also in the haemoglobin level was observed in 4 patients in the series.

Of 15 patients with Hodgkin's disease, of whom 13 had previously had other forms of treatment, only 3 showed no alleviation of symptoms and one of these died 3 days after receiving the first dose. Of 17 patients with acute leukaemia 11 showed no clinical response, but in the remainder there were partial remissions. The drug was ineffective against chronic granulocytic leukaemia, but of 5 patients with lymphosarcoma and chronic lymphocytic leukaemia there was a marked response in 4 and the tumour disappeared in one. Inone of 4 cases of reticulum-cell sarcoma there was an almost complete remission, but no response in the other 3. In one case of rhabdomyosarcoma the tumour disappeared completely. No response, however, was obtained in cases of multiple myeloma, hepatoblastoma. neuroblastoma, renal embryoma, and osteogenic sarcoma. A number of illustrative cases are described in

It is concluded that Hodgkin's disease appears to be the condition most sensitive to the drug and in early cases almost complete remission may be obtained. Anaplastic tumours may show temporary oncolytic changes. However, it is noted that so far the relief obtained has been of short duration and in most cases the effect on tumour tissues has been "less than complete".

: Anne Tothill

569.' Chemotherapy and Chemopraxis of Cancer, 1961 J. F. HOLLAND. Cancer Research [Cancer Res.] 21,

Infectious Diseases

570. Clinical and Epidemiological Observations on Bornholm Disease. (Klinische und epidemiologische Beobachtungen bei Bornholmer Krankheit)

H. TRUCKENBRODT. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 86, 2055–2060, Oct. 27, 1961. 3 figs., 12 refs.

Bornholm disease, which is due to Coxsackie virus, Type B, occurs in small or large epidemics, is most common in summer and autumn, and is frequently confined to a single locality. The study here reported from the University Kinderklinik, Erlangen, was based on 53 cases (46 in children and 7 in adolescents and adults) collected between June and August, 1960, in Coburg and the surrounding district. The total number of cases was probably twice as great, since the disease is not notifiable and the symptoms are often mild.

The onset of the disease is acute with fever and muscle pain which usually affects the intercostal and abdominal muscles and may therefore mimic an acute thoracic or abdominal emergency. Indeed the first 3 children affected were thought to be suffering from acute appendicitis. Since infection is by direct spread, several members may be affected in the same family, often within 48 hours; in one household 5 cases occurred. Symptoms subside just as rapidly, although in some cases recovery may be delayed by recrudescences which, though not as acute as the initial attack, may prolong the illness to a duration of several weeks. Several mothers noted that their children, previously poor eaters, developed a voracious appetite with the fall in temperature, but reverted to their former habits within 4 or 5 days. It is emphasized that the diagnosis of Bornholm disease is not difficult once it is realized that an epidemic is present. D. Preiskel

571. Eplleptic Fits in Acute Anterior Pollomyelitis. (Les crises épileptiques au cours de la poliomyélite antérieure aiguë)

M. Janbon, P. Passouant, and A. Bertrand. World Neurology [Wld Neurol.] 2, 945–953, Nov., 1961. 5 figs., 12 refs.

This paper reports 8 cases of epileptic fits occurring in a series of 58 patients with respiratory complications due to poliomyelitis treated at the Regional Centre for the Treatment of Poliomyelitis, Montpellier, France. The ages of 6 patients ranged from 5 to 13 years, the remaining 2 being 19 years and 24 years old respectively. The clinical types of poliomyelitis represented included the supramedullary (2 cases), bulbar (4), and bulbospinal (2). The epileptic episodes occurred within the first 3 months of the illness in 5 cases and 1 to 4 years afterwards in 3. There were 4 deaths.

Grand mal was the commonest type of fit, but 2 patients had Jacksonian attacks. Electroencephalography was performed in 5 cases. Localized slow waves, mostly

temporofrontal in site, were noted before the Jacksonian fits occurred, but regressed after a few weeks. Generalized abnormalities were less marked and were rarely epileptiform in type. Other clinical neurological signs were common in the early cases, either preceding or following the fits, and were extrapyramidal, with abnormal movements and facial tremor, or sensory, with lower ing of visual acuity. The vegetative derangements frequently accompanying respiratory poliomyelitis were also commonly observed—hypertension, hypotension, tachycardia, bradycardia and circulatory collapse (cyanosis with cold extremities), thermal instability, and dilatation of the stomach.

In 2 cases the fits occurred on the first day of the illness, during an episode of hyperthermia, tachycardia, and hypersecretion of saliva. In 2 cases in which the fits occurred between the 19th and 70th days they were associated with tachycardia, bradycardia, and hypertension, death supervening in both during a convulsion. In 3 cases the fits occurred when, after a varying period of stability, a period of hypertension, tachycardia, and dilatation of the stomach supervened.

The authors consider that fits occurring early in the course of poliomyelitis are related to autonomic and circulatory derangement developing in cases of bulbar palsy with assisted respiration and are probably due to cerebral anoxia and not to poliovirus. Fits occurring later, after months or years, are generally triggered off by respiratory difficulties (hypoxia or hypercapnia). Lesions of the cerebral cortex and reticular formation seem to predispose to fits.

[An interesting paper, emphasizing the importance of maintaining respiratory equilibrium in patients with chronic respiratory insufficiency.]

I. M. Librach

572. Efficacy of Live, Attenuated Measles-virus Vaccine Given with Human Immune Globulin: a Preliminary Report

J. STOKES JR., M. R. HILLEMAN, R. E. WEIBEL, E. B. BUYNAK, R. HALENDA, and H. GOLDNER. New England Journal of Medicine [New Engl. J. Med.] 265, 507-513, Sept. 14, 1961. 11 refs.

Undesirable reactions, such as pyrexia and rash, may follow vaccination of children with live attenuated measles-virus vaccine and may be modified by administration of human γ globulin (McCrumb et al., Amer. J. Dis. Child., 1961, 101, 708; Abstr. Wld Med., 1961, 30, 363). The present authors studied the efficacy of such combined active and passive immunization in relation to measles-virus antibody response and protection against natural measles.

Vaccination of children in Haverford Township, Philadelphia, none of whom had a history of measles, was carried out between December 7, 1960, and February 25, 1961. Alternate children received subcutaneously 0.25 ml. of live attenuated measles-virus vaccine (test group) or fórmalin-killed measles virus vaccine (control group). Immediately afterwards, all the children were given an intramuscular injection of standardized human immune globulin (0.02 ml. per lb. (0.044 ml. per kg.) body weight). A total of 562 children (297 in the test group and 265 controls), aged 1 to 12 years, lived with their families, while 43 (21 in the test group and 22 controls), aged 1 to 3 years, lived in an institution.

Before vaccination 87% of all the children were seronegative (that is, they were measles-susceptible). Examination of serum samples from the test group taken 28 days after vaccination showed that (1) complementfixing antibodies had developed in 98% of the children living at home and in 100% of the children in the institution with, respectively, mean titres of 1:71 and 1:237; and (2) neutralizing antibodies had developed in 99% of the children living at home and in 100% of the children in the institution with, respectively, mean titres of 1:10 and 1:22. The mean neutralization titres were lower than those normally observed following natural measles. Only 5% of the children in the control group developed complement-fixing antibodies, indicating that killed virus vaccine with globulin was poorly antigenic; the results of neutralizing antibody titrations for this group were not available.

The protective efficacy of vaccination by the two methods was tested during epidemics of measles in the ensuing months up to June, 1961. Following intimate exposure, none of 84 children in the test group developed measles—that is, protection was 100%; on the other hand, 68 (94%) of 72 children in the control group contracted the disease. Clinical records after vaccination showed that only 2% of children in the test group developed a rash. In the institution pyrexia (101 to 104.9° F.; 38.3 to 40.46° C. during the 5th to 12th days after vaccination) was observed in 47% more children given live-virus vaccine than in controls; in the children ... living at home fever occurred in 14% more of those in the test group than in the control group. The duration of pyrexia was found to be longer by 2½ to 4½ days in children given live-virus vaccine than in the control Joyce Wright group.

573. Etiology of Cat-scratch Fever

G. L. BOYD and G. CRAIG. Journal of Pediatrics [J. Pediat.] 59, 313-317, Sept., 1961. 17 refs.

The actiology of cat-scratch fever has been, up to the present time, rather obscure. The cat itself is never affected by the disease and an infective agent has never been discovered in its claws, saliva, or teeth. Erythema nodosum has been reported at the onset of the disease and a high percentage of patients with cat-scratch fever manifest tuberculin sensitivity, usually of a low order. Although tuberculous actiology can be ruled out, the possibility of infection with atypical acid-fast bacilli has not been eliminated. These organisms are not tubercle bacilli, but they produce a low-grade tuberculin sensitivity in man and animals.

At the Hospital for Sick Children, Toronto, the authors have found in 8 patients with cat-scratch disease an

increasing number of atypical acid-fast organisms in the lymph nodes and other tissues. Their staining characteristics precluded their being tubercle bacilli. In 7 out of the 8 cases they proved to be atypical acid-fast bacilli of the photochromogenic group. The catalase and peroxydase tests, animal inoculations, and drug sensitivity confirmed the cultural findings.

The authors postulate that a photochromogenic acidfast bacillus may prove to be the aetiological agent in cat-scratch disease. Franz Heimann

574. Recurrence of Staphylococci of Same Phage-type following Control of Nasal Carriers with Neobacrin and Soframycin

A. W. JARVIS and R. D. WIGLEY. Lancet [Lancet] 2, 1168-1170, Nov. 25, 1961. 13 refs.

From Palmerston North Hospital, New Zealand, the authors report a comparison of the efficacy of "neobacrin" ointment and "soframycin" spray in the control of nasal carriers of staphylococci. Before the beginning of the study 60 strains of Staphylococcus aureus, isolated from lesions in patients and staff in the course of routine laboratory work, were tested for resistance to soframycin and were found to be sensitive. Examinations were made of nasal swabs from the nursing staff of 300. Out of 110 nurses whose swabs yielded Staph. aureus, 90 were selected at random and allocated to 3 treatment groups; 66 of these 90 nurses yielded 2 successive positive swabs immediately before treatment and the remaining 24 were excluded from the trial.

The 3 treatments consisted in: (1) neobacrin ointment containing neomycin 5 mg. and bacitracin 500 units per g.; (2) soframycin spray containing framycetin 1.25% and gramicidin 0.005% in buffered isotonic saline, without decongestant; and (3) isotonic saline solution as a control. The treatment was used by the nurse 3 times daily for 7 days. Neobacrin was applied with a swab toboth anterior nares and soframycin and saline were each applied with a nebulizer into each nostril twice at each treatment; swabs were taken immediately before treatment, the day after cessation of treatment, and 12 days after cessation of treatment. The phages used in the study were: Group I-29, 52, 52A, 79, and 80; Group II—3A, 3B, 3C, 55, 71; Group III—42E, 6, 7, 47, 53, 54, 75, and 77; Group IV-42D; and miscellaneous-187, 81, A77.

It was demonstrated, that nasal staphylococci were effectively suppressed by either active preparation while the application was continued, but laboratory studies showed a high rate of recolonization with staphylococci of the same phage type after cessation of both treatments. This suggests that the original organism had survived and that neither treatment will produce complete elimination of the carrier state.

R. G. Meyer

575. Suppression of Nasal, Skin, and Aerial Staphylococci by Nasal Application of Methicillin

D. T. VARGA and A. WHITE. Journal of Clinical Investigation [J. clin. Invest.] 40, 2209-2214, Dec., 1961.

Tuberculosis

576. Calcium Pantothenate in the Clinical Control of Side-effects from Streptomycin. (Пантотенат нальция в клинике туберкулеза при побочном действии стрептомицина)

E. S. STEPANIAN and B. JA. STUKALOVA. Советская Медицина [Sovetsk. Med.] 25, 90-94, Sept., 1961.

The effective treatment of tuberculosis demands prolonged courses of antituberculous drugs such as streptomycin, "phthivasid", and PAS. These agents, however, often cause serious side-effects, such as vertigo, muscular incoordination, and coronary spasm, besides allergic reactions, and it has been reckoned that some 2 to 3% of patients have to suspend or cease treatment owing to these reactions. In an attempt to combat this problem pantothenic acid has been employed, but reports on its effects are conflicting.

In the present study 43 adults with various types of tuberculosis who had shown severe reactions to streptomycin were treated at the Tuberculosis Institute of the U.S.S.R. Ministry of Health with calcium pantothenate in a dosage of 100 to 800 mg, daily, administered in two oral doses or by intramuscular injection of a 20% solution. In only 6 of these patients was it possible to discontinue this treatment after 20 to 30 days without a recurrence of the side-effects to streptomycin; however, in 30 of the remainder the continued administration of pantothénate permitted streptomycin treatment to be maintained, where otherwise it would have been necessary to suspend it. The allergic manifestations were little affected by calcium pantothenate, but the more serious reactions such as vestibular disturbances, headache, and coronary spasm were prevented. Calcium pantothenate in itself produces no unpleasant side-effects; and it does not diminish the bacteriostatic effect of streptomycin either in vitro or in vivo. Its mode of action is as yet undetermined, but it is suggested that in some way it increases the cell content of co-enzyme A, so removing. metabolic disturbances which may be responsible for the side-effects. The authors do not accept the view that it acts by diminishing the combination of ionized calcium with streptomycin, as advanced by Keller, but admit as a possibility Serebrovski's suggestion that it may play some part in the endogenous synthesis of corticosteroids. L. Firman-Edwards

577. Preventive Effects of Isoniazid in the Treatment of Primary Tuberculosis in Children

F. W. MOUNT, and S. H. FEREBEE. New England Journal of Medicine [New Engl. J. Med.] 265, 713-721, Oct. 12,, 1961. 2 figs.

A controlled trial, organized by the U.S. Public Health Service, to determine whether isoniazid could prevent the development of complications in children with primary pulmonary tuberculosis, has been carried out in cities throughout the U.S.A., as well as in San Juan (Puerto Rico), Toronto, and Mexico City. The present report is concerned with 2,750 children admitted to the investigation between January, 1955, and June, 1957. Approximately half the children (1,394)—selected by random sampling-received isoniazid pills providing a dosage of 4 to 6 mg. per kg. body weight per day, and the remainder (1,356) placebo pills; neither the children, their parents, nor the clinic staff knew which children received isoniazid and which the inert placebo. Treatment was prescribed for 12 months, and nearly 75% of the patients completed the full course and over 90% took the pills for at least 6 months. Children with symptomatic disease were excluded, and although the criteria for admission to the investigation were a positive tuberculin test (minimum diameter of induration 5 mm. following 5 units of tuberculin) and radiological evidence of primary tuberculosis, yet in 40% of the children accepted the chest x-ray appearances were normal, but Mantoux conversion in such children was "recent". Clinical examination was carried out on entry to the trial and at monthly intervals during the first year. Chest radiographs were taken initially and again 1, 3, 6, and 12 months thereafter, but during the following 2 years clinical examination was carried out less frequently and radiography performed yearly. An independent panel of radiologists was responsible for assessing the x-ray films.

The two groups of children, who were aged from one to over 11 years, were similar in respect of age, sex, race, environment, and initial x-ray appearances, hilar or paratracheal abnormalities being present in 29.2% of the isoniazid group and 25'9% of the control group, and parenchymal lesions in 16.5% and 19.6% respectively. The incidence of intercurrent respiratory infection and contagious diseases was similar in the two groups. During the year of medication 4 children receiving isoniazid and one in the control group died, while in the next? 2 years 3 in each group died, all from causes unconnected with tuberculosis. The over-all results of the investigation was studied by a "complications review board" consisting of 6 members, each of whom reviewed independently the clinical, radiological, and laboratory findings for each suspected tuberculosis complication, always without knowing which medication the child had received.

It was found that 30 of the 1,394 children treated with isoniazid and 46 of the 1,356 controls given the placebo developed adverse pulmonary changes during the year of medication; this difference is statistically of "borderline" significance. Extrapulmonary complications developed during the first year in only 6 treated children but in 33 of the controls, this difference being highly significant. Further examination of the data showed that the risk of extrapulmonary complications increases with the extent of the radiological involvement and decreases with age.

After the initial treatment year complications developed in a further 4 children who had received isoniazid and in 8 given the placebo. It is concluded that treatment with isoniazid not only suppresses complications at the implantation site, but also prevents such complications by interfering with haematogenous dissemination of tubercle bacilli from the primary lesion. The long-term effects will be observed later, since it is planned that the children are to be seen annually until they are 20 years of age.

[This well-designed and ably executed clinical trial is a most valuable contribution to the literature of primary tuberculosis and proves the undoubted value of isoniazid as a prophylactic drug.]

R. M. Todd

DIAGNOSIS AND PROPHYLAXIS

578. The Use of Chemotherapy as a Public Health Measure in Tuberculosis

COMMITTEE ON THERAPY OF THE AMERICAN THORACIC SOCIETY. Archives of Environmental Health [Arch. environm. Hlth] 3, 441–443, Oct., 1961.

In this statement the Committee lays down the following minimum standards for the drug treatment of outpatients with tuberculosis.

Isoniazid is the most potent drug presently available and whenever antituberculosis chemotherapy is indicated the patient should receive this drug in a minimum dosage of 5 mg. per kg. body weight daily. The minimum duration of continuous treatment with isoniazid should be 12 months, but in most instances it should be continued for 18 months, or at least for "6 months beyond all evidence of activity of the tuberculous process". In selected patients the period of chemotherapy may be prolonged for an indefinite period. "Whenever initial antituberculous chemotherapy is being given for overtly active (bacteriologically positive) tuberculosis a combination drug should be given concurrently. The most commonly used second drug is para-aminosalicylic acid. which may be given in a dosage of 10 to 12 g. daily of the standard product or 6 g. a day of the combinationwith ascorbic acid. If serious drug toxicity or hypersensitivity develops the patient should be admitted to hospital for evaluation of the status of his disease". \ Isoniazid may be used alone in certain circumstances listed below.

Chemotherapy is mandatory in cases of active tuberculosis. It is strongly indicated in: (1) Tuberculin-positive children under 3 years of age. (2) Patients with previously diagnosed tuberculosis in whom activity is uncertain or shown only by minor changes demonstrable on serial radiographs even in the absence of symptoms and bacteriological evidence of disease: This group, would include many subjects "now carried as 'inactive' on tuberculosis registers', who constitute one of the largest unrecognized reservoirs of tuberculosis in the population today. (3) Tuberculin-positive subjects receiving corticosteroids. (4) Tuberculin-positive individuals with radiologically inactive pulmonary lesions who are to undergo gastrectomy. (5) Diabetics with unstable or

severe disease who are tuberculin positive. (6) Patients with nodular silicosis and a positive tuberculin reaction. A strong tuberculin reaction has a bearing on the indications for chemotherapy in this group.

Chemotherapy is discretionary in: (1) Household contacts of patients with positive sputum, regardless of age. (2) Tuberculin-positive children under 14 years old. (3) Subjects giving a positive tuberculin reaction and with pulmonary lesions "for which careful diagnostic study has failed to reveal evidence of another disease". (4) Children with a positive tuberculin reaction who have severe viral infections, especially measles. (5) Pregnant women with inactive tuberculosis. Treatment should be started in the last trimester and should be continued for several months after delivery. (6) A definite conversion from a negative to a positive reaction to 5 t.u. in an adult.

579. Tuberculin Sensitivity and Tuberculosis in Nursing and Medical Students

J. R. KARNS. Diseases of the Chest [Dis. Chest] 40, 291-301, Sept., 1961. 2 figs., 16 refs.

This report is based on the records of 2,497 medical and 1,223 nursing students entering the University of Maryland Schools of Medicine and Nursing, Baltimore, between 1934 and 1959. More than 90% of the medical students were tuberculin tested on entry and non-reactors. at least once a year thereafter. All were subjected to x-ray examination of the chest on entrance and, since 1948 in the case of senior students, at the end of the school year also. In students who were tuberculin positive on entry chest radiographs were obtained annually and in those showing conversion every 3 months for one year, then annually thereafter. The records of nursing students were incomplete for tuberculin testing in 1942 and from 1954-to 1957 but in all of them chest radiographs were obtained before graduation. Routine B.C.G. vaccination was not carried out.

In 1934 65.4% of medical students entering the school were reactors. This figure steadily declined, and since 1950 fewer than 21% were reactors on entrance. The percentage showing conversion declined from 12.7 annually between 1934 and 1939 to 3.8 between 1955 and 1959. Of medical students entering in 1934, 84% were reactors on graduation, while of those graduating in 1959 only 24% were reactors.

Of nursing students entering in 1934, 50% were reactors compared with only 5% in 1959; since 1949 the annual percentage of reactors has been 18. The annual conversion rate fell from 34% between 1934 and 1939 to 1.5% in the years 1958 and 1959. At the end of the 3-year training course 92% of nursing students who had entered in 1934 were positive reactors, whereas only 13% of those leaving in 1958 were positive reactors and they, incidentally, had spent one year less in hospital.

Between 1934 and 1950 clinical pulmonary tuberculosis was diagnosed in 16 medical students—5 out of 747 who were reactors on entry and 11 of 873 non-reactors, giving attack rates of 6.69 and 12.49 per 1,000 respectively. Only one case was diagnosed after 1950. An extrapulmonary lesion, a hand chancre, developed in a stu-

dent handling tuberculous cadavers at necropsy. Among the nurses there were 9 cases of tuberculous disease between 1934 and 1948; there have been none since.

[In the light of these figures the present value of B.C.G. inoculation must be reconsidered.]

Janet O. Ballantine

RESPIRATORY TUBERCULOSIS:

580. Rest, Exercise, and Work in the Treatment of Tuberculosis

COMMITTEE ON THERAPY OF THE AMERICAN THORACIC Society. Archives of Environmental Health [Arch. environm. Hlth] 3, 438-440, Oct., 1961.

The Committee on Therapy of the American Thoracic Society recently considered the place of rest and hospitalization in the treatment of tuberculosis. In the Committee's yiew patients who are bacteriologically positive and have symptoms can benefit from rest in bed during the greater part of the day, and patients bacteriologically positive but symptomless should normally be confined "to the ward area because of their infectiousness". Patients who are bacteriologically negative and have no symptoms may be discharged from hospital to continue chemotherapy and be followed up as outpatients. Hospitalization may be necessary if the patient is considered unreliable or the social and economic environment is unfavourable; for those who remain in the hospital full activity is recommended and freedom should be granted to visit all areas of the hospital available to general hospital patients. Occasional visits outside the hospital with family or friends should be

"This Committee still believes that initial hospitalization of tuberculous patients is necessary, even when rest in bed is not indicated. Confinement in a tuberculosis or general hospital during the initial phases of treatment is important for the following reasons: (1) Isolation of the patient is assured while he is still bacteriologically positive or while the bacteriological status is being established. (2) Superior diagnostic facilities are available for establishing the complete diagnosis. (3) Chemotherapy may be initiated while the patient is under careful observation for possible toxic manifestations. (4) The necessity for surgery may be adequately assessed. (5) Education and reassurance of the patient concerning his disease may be accomplished. (6) The adequacy of social and economic conditions for continued post-A. J. Karlish hospital therapy can be assessed."

581. Toxic and Allergic Drug Reactions during the Treatment of Tuberculosis

J. M. SMITH and M. H. ZIRK. Tubercle [Tubercle (Lond.)] 42, 287-296, Sept., 1961. 5 figs., 12 refs.

Toxic and allergic reactions during the treatment of tuberculosis were studied at the Chest Clinic and 4 hospitals in Birmingham in 628 new cases of the disease seen between February, 1958, and January, 1959, and followed up for 12 months. Most of the patients received streptomycin, PAS, and isoniazid together initially, and in various combinations later. Cycloserine, pyrazinamide, and ethionamide were not given. Isoniazid was given to all the patients, the standard dose being 200 mg. daily in adults, although some had 300 mg. and a few 400 mg. All except 5 patients were treated with PAS, 74% of the patients receiving this drug for 12 months. The dosage of PAS varied from 10 to 20 g. a day in adults but was less in children. Streptomycin was given to fewer patients (544) than either of the other two drugs and only 7.4% received it for a year. The dosage was 1 g. daily, less in children.

Allergic reactions—that is, rashes, fever, and asthma produced within a few hours by a single dose of a drugwere due to streptomycin in 44 patients (8% of those at risk) and to PAS in 54 (8.7% of those at risk). No allergic reactions to isoniazid were observed. The majority of these reactions occurred within the first 6 weeks of treatment with either drug. Reactions to both drugs occurred in 23 (5%) of the 472 patients who received them for at least 6 weeks. Desensitization was satisfactory in the treatment of reactions in almost all cases; provided the initial dosage of either PAS or streptomycin was 0.01 g. increasing by 0.01 g. daily to 0.1 g. and thereafter by 0.1 g. daily to 1 g. daily; and, in the case of PAS, by a further 1 g. daily to the desired dose. Where sensitivity tended to occur on this regimen prednisolone (at least 20 g. daily) was administered for the whole period of desensitization, the dosage being slowly reduced over the following month.

Toxic reactions, such as vertigo and deafness with streptomycin, and nausea, vomiting, and diarrhoea with PAS, were specific for the drug and not usually reproducible by a single test dose or responsive to desensitization. In 44 (8%) of the patients receiving streptomycin vertigo occurred and treatment had to be stopped. In only 3 (0.5%) was PAS discontinued because of gastrointestinal symptoms. Isoniazid caused no toxicity.

It is pointed out that the importance of toxic and allergic reactions must be judged from the fact that in 122 (20%) of the patients a toxic or allergic reaction occurred which caused interruption of the planned treatment either temporarily or permanently. "The completion of successful treatment depended in many cases upon the skill of the physician in overcoming the allergic type of reaction by means of desensitization". Children were remarkably-free from both toxic and allergic reactions, but both types were twice as common in women as in men. Skin tests as an index of allergy were unreliable.

It is concluded that admission to hospital may be desirable for at least the first 5 or 6 weeks of treatment so that allergic reactions, which can be expected in 12% of patients, can be identified and treated.

W. Raymond Parkes

582. Drug Resistance in Untreated Pulmonary Tuberculosis in England and Wales during 1960

A SURVEY BY THE PUBLIC HEALTH LABORATORY SERVICE. Tubercle [Tubercle (Lond:)] 42, 308-313, Sept., 1961.

During 1960 23 laboratories of the Public Health Laboratory Service in England and Wales submitted to the Tuberculosis Reference Laboratory strains of mycobacteria isolated from sputum or gastric contents of patients aged 15 years or over who were newly diagnosed cases of pulmonary tuberculosis and who had received chemotherapy for less than 2 weeks. Drug-resistant strains and any considered to be "anonymous" mycobacteria were inoculated into guinea-pigs, while the identity of 6 bovine strains was confirmed by inoculation in rabbits. Sensitivity tests were carried out on Löwenstein-Jensen egg medium containing streptomycin, isoniazid, and PAS in various concentrations; isoniazid-resistant strains were tested for the presence of catalase. "Anonymous" mycobacteria were identified by their growth at 25° C., together with either their resistance to thiosemicarbazone or their pigmentation, or both.

A total of 1,371 strains were analysed. The over-all incidence of primary resistance to any of the drugs tested was 3.1% (2.1% resistant to streptomycin, 1.0% to PAS, and 1.0% resistant to isoniazid). The incidence of isolation of "anonymous" mycobacteria in relation to new cases of tuberculosis was 1.9%, and of those considered to be probable pathogens was 1.0%. It is concluded that the incidence of primarily resistant cases in the present survey (3.1%) does not differ significantly from that found in the previous survey in 1955-6 (3.4%). There has been an increase since that time of primary isoniazid-resistance from 0.6% to 1.0%. From a comparison with the results of surveys reported from other countries it is concluded that the prevalence of drug resistance in tuberculosis is less in Britain than in those countries. John M. Talbot

583. Choice of Initial Chemotherapy Regimen in Pulmonary Tuberculosis

A. SALIBA and O. A. BEATTY. Diseases of the Chest [Dis. Chest] 40, 259-264, Sept., 1961. 15 refs.

The authors set out to demonstrate the importance of adequate initial chemotherapy in the treatment of pulmonary tuberculosis. Since November, 1958, patients admitted to hospital without previous treatment or treatment for less than 3 months and with sputum positive for tubercle bacilli were given a high dosage of isoniazid of 16 mg. per kg. body weight daily (usually 800 to 900 mg. daily), together with streptomycin in a dosage of 1 g. daily. After 4 months streptomycin was replaced by 10 to 20 g. daily of PAS. Pyridoxine, 50 to 199 mg. daily, was also given.

The results obtained in 60 consecutive patients who had completed 6 months' treatment are described. Most of the patients had far-advanced disease and extensive cavitation, over half having multiple cavities. In 12 cases there was some degree of drug resistance at the time of admission and PAS was added to the treatment regimen. Sputum conversion was obtained without surgery usually in the first 3 months in all the patients with a drug-susceptible infection at the start, and in all except one of the 12 with some initial resistance. Although some toxic symptoms were observed in a few cases, these did not necessitate cessation of treatment. Radiologically 55 patients improved and none deteriorated, although cavity closure "was not often obtained".

Janet Q. Ballantine

584. The Rehabilitation of Chronic, Drug Resistant Cases of Tuberculosis with Cycloserine, and Successful Treatment of Virgin Cases

I. G. Epstein, K. G. S. Nair, M. G. Mulinos, E. Horiuchi, and B. Encarnacion. Diseases of the Chest [Dis. Chest] 40, 276–283, Sept., 1961. 18 refs.

The authors describe their experience of cycloserine, alone or in combination with isoniazid, in the treatment of 397 patients with pulmonary tuberculosis seen at the Metropolitan Hospital, New York. Cycloserine was administered in divided doses to a total of 0.5 g. to 2 g. daily, the aim being to maintain a plasma level of 30 to 50 mg. per ml. to prevent neurotoxic damage. Pyridoxine was also given since the authors have found that the concomitant administration of this drug allowed "an increase in the dosage of cycloserine, with a minimum risk of toxic reactions". With this regimen toxic reactions were rare, and resistance to cycloserine even after years of continuous therapy was an infrequent occurrence and never complete.

Of 139 patients with drug-resistant, far-advanced cavitary disease 114 were given cycloserine alone and 25 received in addition 300 to 600 mg. of isoniazid daily. The results obtained with the combined drugs did not "differ in any way" from those obtained with cycloserine alone. Similar results have been reported by other workers.

Of 258 patients with previously untreated pulmonary tuberculosis 44 received cycloserine alone and 214 received isoniazid in addition. More than two-thirds of these patients had cavities. In 16 patients with advanced cavitary disease given cycloserine alone the sputum conversion rate after treatment for 12 weeks was 62%. Radiologically improvement was slight in one patient, moderate in 9 patients, and marked in 5; the condition in one patient deteriorated. In all the patients sputum volume was reduced, cough was virtually absent, and temperature became normal. Of 75 patients treated for a full year 71 showed marked to moderate improvement with sputum conversion [rate not given], clinical and radiological improvement following parallel courses.

[The figures given in this article are unsatisfactory—for example, a table gives 62 patients on cycloserine and isoniazid after one year with a sputum conversion rate of 56%, yet see the above figures taken from the text.]

Janet Q. Ballantine

585. The Treatment of Tuberculous Patients with Cycloserine. (Лечение больных туберкулезом циклосерином)

D. D. Aseev and S. R. Lačinian. Проблемы Тубер-кулева [Probl. Tuberk.] 39, 20–27, No. 7, 1961. 6 refs.

The authors report that of 102 patients treated with cycloserine, which they have found to be an effective preparation for the treatment of chronic tuberculosis, clinical amelioration was observed in 60.8%. They point out that it is essential to administer cycloserine along with some other preparation and in their experience the best combination is that with phtivazid or one of its analogous preparations. Given in doses of 0.75 to

1 g. daily cycloserine was in general very well tolerated, even by patients receiving a prolonged course of treatment. However, in 5.5% of cases the drug was poorly tolerated during the first few days of treatment, the side-effects occurring in 15 patients including headaches, vertigo, incoordination of gait, and paraesthesiae, these mostly resulting from disturbances in the central nervous system; some of these effects could be counteracted by large doses of vitamin B₁ (aneurine). Side-effects occurred in 19.6% of patients. The authors conclude by emphasizing that cycloserine should be resorted to only after all the ordinary antituberculous preparations have proved ineffective or when the patient has developed a resistance to streptomycin, phtivazid, and PAS.

H. W. Swann

586. An Assessment of Antibacterial Treatment used Alone or in Association with Surgical Operation in the Treatment of Pulmonary Tuberculosis

J. R. EDGE, W. H. HELM, M.-R. GEAKE, and R. L. WARD. *Thorax* [*Thorax*] **16**, 256–263, Sept., 1961. 4 figs., 29 refs

The results obtained with antibacterial drugs alone or in association with surgery in the treatment of pulmonary tuberculosis were assessed in 390 patients with cavitary disease and a positive sputum seen between January, 1954, and December, 1956, at hospitals in the area of the Manchester Regional Hospital Board. Of 97 patients in whom cavity closure was followed by resection or thoracoplasty, 96 were alive (one non-tuberculous death); none of the patients in this group had a relapse. Of 185 patients with cavity closure following antibacterial treatment alone 3 had a relapse and 9 died from causes other than tuberculosis. In the remaining 108 patients, who had persistent cavitation and a negative sputum, surgery was not carried out; these patients had more extensive disease and were older than the other patients in the series. In this group relapse occurred in 3 patients, one of whom died from tuberculosis; and there were 7 non-tuberculous deaths. The authors state that in all the patients sputum converted to negative within 6 months of starting treatment and that the relapses occurred in those who had been given unsatisfactory antibacterial treatment in the early stages. Pulmonary heart disease was the cause of 8 deaths in the series.

The authors conclude that there is nothing to be gained from "insurance" surgery in patients with closed cavities and negative sputum after antibacterial treatment for 6 months, provided the bacteria were initially sensitive and adequate treatment is maintained for at least 18 months.

I. Ansell

587. Effect of Direct Irradiation on the Course of Pulmonary Tuberculosis (Using Cancerocidal Doses)
I. D. Bobrowitz, M. Elkin, J. C. Evans, and A. Lin.

Diseases of the Chest [Dis. Chest] 40, 397-406, Oct., 1962. 8 figs., 13 refs.

In this study the primary objective of the authors, working at the Bronx Municipal Hospital Center, New York, was to determine whether there is any hazard in the use of irradiation to the thorax for neoplastic disease

co-existent with pulmonary tuberculosis. Because of the increased longevity of patients with tuberculosis the two conditions are becoming prevalent in the same age and sex group, namely, the older man.

In a preliminary study of the effect of irradiation on 8 patients with pulmonary tuberculosis in 1953 and 1954 it was found that, under cover of antituberculous drugs, radiotherapy with small and moderate doses could be administered without danger of deterioration of the tuberculosis. The present study was therefore planned with the use of much larger doses of x rays for the treatment of inoperable lung cancer associated with pulmonary tuberculosis. Seven patients were so treated between December, 1956, and November, 1958, and full details of each case are given. No clinical or x-ray evidence of relapse of tuberculosis was found in 6 cases. In the 7th the patient had discontinued antituberculous drug treatment; moreover, the changes seen might have been due to radiation necrosis. The total period of observation after irradiation varied from 7 weeks to 321 months. Norman F. Smith

588. A Controlled Trial of Calcium B-PAS

A. W. Lees and G. W. Allan. British Journal of Diseases of the Chest [Brit. J. Dis. Chest] 55, 185-191, Oct., 1961. 11 refs.

This paper describes a controlled trial designed to compare calcium B-PAS (calcium benzamidosalicylate) and sodium PAS for their effectiveness in preventing the emergence of drug-resistant tubercle bacilli. For this purpose patients admitted to Ruchill Hospital, Glasgow, between December, 1958, and June, 1960, with active, previously untreated pulmonary tuberculosis were given treatment consisting in the administration of 12 cachets daily giving a dose of 400 mg. of isoniazid together with (Group A) 15 g. of sodium PAS or (Group B) 15 g. of calcium B-PAS, patients being allocated to the 2 groups alternately. Chest radiography and culture of sputum were carried out at 3-monthly intervals. Initially each group contained 66 patients, but withdrawal of those whose sputum was bacteriologically negative and those in whom the organisms were found to be resistant to either drug left Group A with 56 and Group B with 53 patients.

After 3 months' treatment 10 patients in Group A remained culture-positive; in 2 cases the organisms were no longer fully sensitive to isoniazid, and in one of these also no longer fully sensitive to sodium PAS. In Group B 8 patients were still culture-positive and in 2 cases the organisms were no longer fully sensitive to isoniazid. At the end of 6 months' treatment in Group A there were 3 patients still culture-positive and in 2 cases the organisms were no longer fully sensitive to isoniazid; in Group B there were 2 patients culture-positive, and in one of these the organism was resistant to isoniazid and in the other to PAS.

From this controlled trial it would therefore appear that calcium B-PAS in a dosage of 15 g. daily proved as effective a companion drug for isoniazid as did sodium PAS in the same dosage.

Kenneth M. A. Perry

Venereal Diseases

589. Venereal Disease in Adolescents
L. WATT. British Medical Journal [Brit. med. J.] 2, 858-860. Sept. 30, 1961. 2 refs.

Venereal disease among young people is one of the anxieties of the moment, and the author has undertaken an investigation of the extent of this problem in the Manchester area. He has limited his investigation to the age group 15 to 19 years and has examined records for the years 1938, 1939, 1949, 1950, 1959, and 1960. The area was served by two clinics, in Manchester and Salford, up to 1954, but they were then amalgamated at St. Luke's Clinic, Manchester. It was therefore necessary to study the records of both clinics for earlier years, but of St. Luke's Clinic only for the last 2 years. The investigation relates to cases of early infectious acquired syphilis and of acute gonorrhoea, the totals indicating numbers of infections and not numbers of individuals. In 1938 the number of infections occurring in males of this age was 39, or 3.1% of the total of 1,227 cases. The proportion rose sharply in 1939 and fell in 1949. In 1959 there were 62 (4.8% of 1,249) and in 1960 56 (4.9% of 1,123) cases in patients of this age group. In 1939 there were 225 infections in females, of which 23 (10.2%) were in patients aged 15 to 19 years. Apart from a fall in 1950, the proportion increased steadily until, in 1959, 75 of 315 infections (23.8%) were in young people of this age, and in 1960 78 out of 329 (23.7%). The increase was not related to an increase in the number of young people in the area, because the totals of males and females aged 15 to 19 in Manchester and Salford in 1938 were 39,665 and 41,617 respectively, and by 1960 had fallen to 27,388 and 27,475 respectively. The proportion of coloured immigrants among these young people was small, but some of the girls had acquired infection by consorting with older coloured males. The author comments that, if it be accepted that trends in venereal disease reflect trends in promiscuity, the conclusion must be that promiscuity among adolescents has increased.

A. J. King

590. X-ray Photography of Unerupted Permanent Teeth in Congenital Syphilis

T. PUTKONEN and Y. V. PAATERO. British Journal of Venereal Diseases [Brit. J. vener. Dis.] 37, 190-196, Sept., 1961. 8 figs., 12 refs.

The authors, writing from the University Hospital, Helsinki, describe the x-ray appearance of unerupted permanent teeth in 42 congenital syphilitics, in 12 of whom they were able to complete follow-up studies after the second dentition. The original ages of the children ranged from 13 months to 6 years, 11 months, with an average of 4 years, 9 months, while the age at follow-up ranged from 8 to 14 (mean 11) years.

The 42 radiographs of unerupted central incisors were classified as follows: definitely syphilitic 13 (31%),

probably syphilitic 9, and normal 20. Of the 12 patients attending for follow-up examination, 7 were from the definitely syphilitic group and all had Hutchinson's teeth (the authors' criteria for which are defined), while the remaining 5 were in the possibly syphilitic group. Of the latter, one had normal upper central incisors, in 2 cases the teeth were doubtfully of syphilitic type, in one they were distinctly syphilitic, while the 5th child had enamel hypoplasia. Only 10 radiographs of unerupted molars were obtained. None showed signs of syphilitic change in first molars, although at follow-up examination a typical Moon's molar was seen in one patient.

There seems little doubt that unerupted syphilitic upper central incisors can be reliably demonstrated radiologically, but similar studies of molars are not rewarding. Antisyphilitic treatment makes no difference to the appearance of affected teeth on eruption. The authors discuss the technical difficulties of obtaining good radiographs of such teeth; they suggest that errors can be reduced by use of the orthopantomograph.

[The illustrations accompanying this paper are very good.]

R. S. Morton

591. The Immobilization Reaction with Reiter's Treponeme. Comparison with the Immobilization Reaction with Pathogenic *Treponema pallidum*. (La reazione d'immobilizzazione del treponema di Reiter. Saggio comparativo con la reazione d'immobilizzazione del *Treponema pallidum* patogeno)

G. D'ALESSANDRO and P. ZAFFIRO. Rivista dell'Istituto sieroterapico italiano [Riv. Ist. sieroter. ital.] 36, 203-211, July-Aug. [received Oct.], 1961. 12 refs.

In a brief preliminary discussion of the *Treponema* pallidum immobilization test the authors, writing from the Institute of Hygiene of the University of Palermo, mention the "pre-lytic" changes which occur in pathogenic *T. pallidum* before the immobilization and also the prolonged exposure to antibody necessary to induce preparedness for immobilization. They then report a study of the immobilization of actively motile-Reiter treponemes by homologous sera and by sera from syphilitic rabbits and patients. The methods of cultivation and other technical details are briefly indicated [but the total number of tests is not given].

Reiter's treponeme, less actively motile than *T. pallidum*, is not immobilized in 18 hours by normal rabbit serum. With anti-Reiter immune serum immobilization begins in one hour and is almost complete in 2 hours, when morphological changes also begin, lysis being almost complete in 12 hours. In contrast immobilization of *T. pallidum* only approaches completeness in 16 to 18 hours with particularly potent sera and morphological changes have by then occurred which correspond to those seen in the Reiter organism in 2 hours. As the

Reiter's treponemes studied were suspended in Brewer's thioglycollate medium and T. pallidum in Nelson-Mayer maintenance medium an immobilization test using T. pallidum suspended in Brewer's medium was carried out. After 6 hours immobilization affected only 16% of the organisms and longer exposure was not possible because T. pallidum does not survive in Brewer's medium.

The results were compared of complement fixation reactions with cardiolipin and Reiter protein antigens and immobilization reactions with Reiter's treponeme and *T. pallidum* against various sera. The main results were as follows:

Type of Serum	Complement Fixation		Immobilization	
	Cardio- lipin Antigen	Reiter Protein	Reiter's Treponeme	Troponema pallidum
Anti-Reiter's treponeme Anti-Reiter protein Anti-lipoid Rabbit syphilitic Human syphilitic Human syphilitic	+++	+ - +	1.1 1 ++	++++

The rapid lysis of Reiter's treponeme compared with the long "preparatory" period preceding the immobilization of T. pallidum is attributed by the authors to the absence from Reiter's organism of a lysozyme-sensitive envelope such as has recently been described on T. pallidum. The specificity of the immobilizing antibody is emphasized: Syphilitic human and rabbit sera, although strongly reacting in complèment fixation tests with the Reiter protein antigen, do not immobilize Reiter's treponeme. The immobilization of Reiter's treponeme by anti-Reiter protein sera must be interpreted cautiously, because traces of lipoid and polysaccharide, of no consequence in tests in vitro, may well lead to the production of antibodies on immunization In vivo.

The authors suggest that this test may be useful in helping in the identification of immobilizing antibody.

F. Hillman

592. Treatment of Gonorrhoea with Phenethicillin (Broxil)

A. L. HILTON. British Journal of Venereal Diseases [Brit. J. vener. Dis.] 37, 207-209, Sept., 1961. 7 refs.

Phenethicillin ("broxil") is a synthetic penicillin, being the potassium salt of 6-(α-phenoxypropionamido) penicillanic acid. Claims that this drug produces blood levels equal to those of penicillin injected intramuscularly prompted the trial of this drug in 66 cases of acute male urethral genorrhoea seen at the Royal Infirmary, Doncaster. Diagnosis was made by examination of smears and culture. All the patients received 2 g. of the drug; 54 being given the dose equally divided at 6-hourly intervals, while the other 12 received the 2 g. in a single dose. The only selection employed was to exclude patients who by history or occupation seemed unlikely to attend for follow-up. The serum penicillin levels were estimated in some cases, and disk sensitivity tests were performed on a solid agar medium.

Of the patients in the two treatment groups 49 and 12 respectively were followed up for 2 weeks, two-thirds for a month, and one-third for 2 months: The failure rate was 46.9% and 58.3% respectively in the 2 groups. There was good correlation between the clinical outcome and the sensitivity tests, although the type of test used is admittedly generally recognized as a screening procedure only. The least sensitive strains contributed 80% of the failures. The studies of serum concentration showed the drug to be well absorbed. Side-effects were limited to diarrhoea in several patients, which in 2 was severe. A comparison of these findings with those achieved with other oral penicillins both in vivo and in vitro suggests that phenethicillin is probably the least useful of these drugs in the treatment of acute gonorrhoea.

R. S. Morton

593. Treatment of Acute Gonorrhoeal Urethritis in the Male with a Single Injection of Oxytetracycline E. M. VANDER STOEP, C. H. MONTGOMERY, and J. M.

KNOX. British Journal of Venereal Diseases [Brit. J. vener. Dis.] 37, 216-218, Sept., 1961. -1 fig., 7 refs.

The comparative efficacy in the treatment of acute gonorrhoea in the male of a single intramuscular injection of oxytetracycline and a single intramuscular injection of 1,200,000 units of penicillin with aluminium monostearate (P.A.M.) was studied at the Venereal Disease Clinic, Houston, Texas. Three dosage schedules of oxytetracycline were used—250 mg. (365 patients), 500 mg. (197 patients), and 250 mg. repeated after an interval of 48 hours (91 patients). P.A.M. was given to 344 patients. Considerable local pain was noted at the site of injection of oxytetracycline in spite of the administration of a local anaesthetic.

The authors conclude, according to the criteria adopted, that a single intramuscular injection of 500 mg. of oxytetracycline is as effective in the treatment of acute gonorrhoea in the male as a single injection of 1,200,000 units of P.A.M., that two injections each of 250 mg. of oxytetracycline are less effective, and that a single injection of 250 mg. is unsatisfactory.

Leslie Watt

594. Treatment of Non-gonococcal Urethritis with Intramuscular Tetracycline (Terramych)

R. S. MORTON. British-Journal of Venereal Diseases [Brit. J. vener. Dis.] 37, 214-215, Sept., 1961.

Intramuscular injections of oxyfetracycline hydrochloride were given at the Royal Hospital, Sheffield, to 48 males suffering from non-gonococcal urethritis, the dosage being 200 mg. daily for 4 days. The diagnosis was established by examination of Gram-stained smears of urethral discharge. A variety of local anaesthetic agents was used to minimize pain after injection, which was severe enough in 7 cases to call for cessation of treatment. Of the 36 patients who completed treatment 32 responded immediately with cessation of symptoms but 5 of these had a recurrence later. It is concluded that the results compare favourably with those obtained with oral tetracycline therapy, but because of local reactions intramuscular injections are not recommended for routine treatment of this condition. Leslie Watt

Tropical Medicine

595. The State of Pyridoxine Nutrition in Patients with Kwashlorkor

J. J. THERON, P. J. PRETORIUS, H. WOLF, and C. P. JOUBERT. *Journal of Pediatrics* [J. Pediat.] 59, 439–450, Sept., 1961. 4 figs., 31 refs.

Although no characteristic syndrome of pyridoxine deficiency has been described in human adults there are accounts in the literature of patients with anaemia which proved refractory to all other treatment until pyridoxine was given. Experimentally, desoxypyridoxine, an antivitamin of the pyridoxine group, has been shown to produce in human subjects a pellagra-like state, with seborrhoeic dermatitis, cheilosis, glossitis, and polyneuritis. Milk deficient in pyridoxine can induce a syndrome of convulsions and abnormal electroencephalograms in infants.

At the National Nutrition Research Institute, Pretoria, South Africa, the authors have studied methods of detecting pyridoxine deficiency in 18 African children with kwashiorkor. On admission to hospital the patients were given a skimmed-milk formula for the first 4 days, after which they received the normal full ward diet. All received 300,000 units of phenoxymethylpenicillin 6-hourly during the first week and a teaspoonful of multivitamin mixture which contained no pyridoxine. In patients suffering from pyridoxine deficiency an abnormal intermediate metabolite of tryptophan, xanthurenic acid, appears in the urine. The administration of a test load of DL-tryptophan has been used experimentally to measure the degree of pyridoxine deficiency. The excretion of xanthurenic acid is high in kwashiorkor and is further increased by the administration of tryptophan. Following a test dose of 0.5 g. of DL-tryptophan per kg. body weight in 13 of the authors' cases it was found that the mean increase in excretion of xanthurenic acid amounted to 14.9 mg. per 24 hours. After 14 days' treatment the increase was still 12.34 mg., after 28 days 8.22 mg., but after 42 days it had fallen to 2.81 mg. per 24 hours; in 3 cases the amount excreted initially had exceeded 30 mg. in 24 hours. It was also shown that the serum glutamicoxalacetic transaminase activity decreased during recovery, the mean value on the 42nd day of treatment being 14.5 (± 7.05) units as against 19.4 (± 13.34) on admission. There were wide variations in individual cases, however, and this criterion is not considered to be of much use in assessing the degree of pyridoxine deficiency.

The urinary excretion of N-methyl nicotinamide after administration of tryptophan increased by up to 8·7-fold in 12 patients examined. The ability to convert tryptophan to N-methyl nicotinamide is lost in pyridoxine-deficient subjects and this test is considered one of the most sensitive in confirming deficiency of the vitamin. The urinary excretion of 4-pyridoxic acid in the authors' cases was low on admission, not exceeding 0·19 mg. in 24

hours in any of the cases. It increased steadily with treatment and after administration of pyridoxine a marked increase occurred, 7 of the patients excreting more than 8 mg. per 24 hours after 42 days in hospital. There were no specific changes in total lymphocyte counts during treatment. The authors conclude that determination of the urinary excretion of xanthurenic acid before and after a test dose of tryptophan provides the most useful index of pyridoxine metabolism in patients with kwashiorkor. William Hughes

596. The Effect of Protein Hydrolysate on Initiation of Cure and Various Biochemical Indices of Recovery in Kwashiorkor

P. J. PRETORIUS and L. S. DE VILLIERS. South African Journal of Laboratory and Clinical Medicine [S. Afr. J. Lab. clin. Med.] 7, 108-113, Sept. [received Nov.], 1961. 29 refs.

Despite the improved outlook in recent years for patients with kwashiorkor, the reported mortality from this disease still ranges from 20% to 60% in various parts of the world, although at Pretoria General Hospital, from which this paper comes, the death rate was in one series reduced to 15%. As well as the dietary deficiency of protein in kwashiorkor it is known that there is also diminished enzyme activity in the intestinal tract. The use of protein hydrolysate has therefore been recommended in initiating cure, and in this study the authors have investigated the effectiveness of this treatment in 58 Bantu infants with kwashiorkor, alternate patients being assigned on admission to the hydrolysate-treated group while the alternands formed a control group. Both groups were given a basic regimen consisting of spraydried reconstituted milk with 3% "dextrinmaltose" added. Severely ill patients received intravenous therapy with penicillin or a broad-spectrum antibiotic where indicated. The experimental group were given a proprietary protein hydrolysate preparation ("nesmida") in a proportion of 2% of the dietary formula and the controls an equivalent amount of casein as "casilan". Five of the infants died soon after admission, before the treatment proper began, 2 were found to be suffering from pulmonary tuberculosis, and in 2 cases plasma and blood transfusions had to be given. Excluding these 9 cases there remained 26 patients in the treated group and 23 controls; however, a further 6 infants, all in the treated group, died during the test period. The authors state that 5 of these patients were severely ill and their deaths are not attributed to the diet given.

Among the 43 surviving patients there was no significant difference between those in the two groups in respect of increase in body weight, serum glutamic-oxalacetic transaminase activity, increased serum amino-nitrogen level, nitrogen balance, or urinary nitrogen partition. It is noted that the mean serum amino-nitrogen level, which

in both groups was 1.8 mg. per 100 ml. on admission, increased in both to 3.9 mg. per 100 ml. after 2 weeks. The apparent absorption of nitrogen from the intestinal tract averaged 86% in the treated group and 88% in the controls. This was an unexpected finding, in view of the known frequency of diarrhoea in kwashiorkor and the comparatively low level of enzyme activity in the intestinal tract.

With these results in mind, coupled with the fact that protein hydrolysates are expensive, the authors conclude that no therapeutic advantage is to be gained by giving these supplements in the acute stage of kwashior-kor.

William Hughes

597. Treatment of Amoebic Dysentery with 4:7-Phenantrolene—5:6-quinone

H. SMITSKAMP and F. M. LALISANG. Tropical and Geographical Medicine [Trop. geogr. Med.] 13, 119-122, June [received Nov.], 1961. 7 refs.

A new synthetic compound, 4:7-phenantrolene-5:6quinone ("entobea") has been shown in preliminary trials to exert a marked amoebicidal effect in animals and in men. At the Harbour Hospital, Institute of Tropical Disease, Rotterdam and Leyden, the authors have treated 26 patients with amoebic dysentery, mostly while confined to bed. In 22 cases there were active amoebae in the stools; in 4 only cysts or minute forms were present, but the clinical signs were typical. The compound was given in doses of 100 mg. 3 times daily for 7 to 10 days. The response was always good. Amoebae disappeared from the stools after 1 to 5 days and cysts disappeared some 5 days later. Symptoms were relieved within 7 days and amoebic ulcerations in the lower bowel healed. The compound was well tolerated. Most patients could not be followed up, but 8 were seen again after 18 to 120 days. One of these had a recurrence of symptoms (mild diarrhoea and cramps), but no amoebae were found and the symptoms cleared up without further treatment.

F. Hawking

598. Mass Treatment of Wuchereria bancrofti Filariasis with Diethylcarbamazine

W. J. O. M. VAN DUK. Tropical and Geographical Medicine [Trop. geogr. Med.] 13, 143-159, June [received Nov.], 1961. 17 refs.

At Inanwatan, Western New Guinea, investigations on 1,206 persons of all age groups showed an incidence of elephantiasis of 8.4% and of all forms of filarial disease of 10.6%. The microfilaria rate was 22% for all persons and 24 to 41% for adults over 20 years. The average microfilaria density for the whole group was 12 to 14 microfilariae per 20 c.mm. of blood at 9 p.m. [These figures show that filarial infection was very heavy.] The chief vector was Culex annulirostris, with Anopheles faranti as a secondary one. C. fatigans was scarce and unimportant. Transmission took place mostly in the food-growing plots.

Mass treatment consisting of diethylcarbamazine citrate (6 mg. per kg. body weight) was given to all the people in the area once every 4 weeks for 12 doses. (This was combined with chloroquine 5 to 10 mg. per kg.

in an unsuccessful attempt to diminish malarial infection.) The population totalled 1,250 persons, and over 95% took at least 11 of the 12 doses. Four weeks after the first dose 20% of the 225 microfilaria carriers had become negative and the microfilaria density was reduced by 72%. Four weeks after the second dose 33% of the carriers had become negative and the microfilaria density had been reduced by 89%. After 12 months the microfilaria rate had been reduced by 94% and the microfilaria density was reduced by 98.7%. Side-effects occurred in 25% of cases after the first dose, early reactions consisting in symptoms such as fever, headache, and aching pains in the body, and sometimes a tender swelling in the groins or knee; late reactions, appearing after 10 to 30 days, consisted in infiltration in the thigh or elsewhere which sometimes led to abscesses. After the second dose only 3 to 4% of persons developed a mild reaction. These reactions did not interfere with the acceptance of treatment.

[This trial was well organized and the report is well documented.] F. Hawking

599. Anaemia and Parasitic Infestation in African Children in Northern Rhodesia

B. Friis-Hansen and F. S. McCullough, Journal of Tropical Medicine and Hygiene [J. trop. Med. Hyg.] 64, 243–250, Oct., 1961. 15 refs.

Results are given of an investigation into the incidence of anaemia and parasitic infestation made during a preliminary survey of 3 areas in Northern Rhodesia, in flat bush country at an altitude of 3,000 to 4,000 feet (915 to 1,220 metres). The annual rainfall is usually 40 to 50 inches (101.6 to 127 cm.) and the temperature range from 54° to 94° F. (12.25° to 34.45° C.). The native population is of Bantu origin. Diets varied somewhat in the 3 areas, but consisted chiefly of maize flour, cassava, and millet together with a small amount of meat or fish. About 1,800 children and 200 lactating women were examined.

In all 3 areas there was widespread, severe hypochromic anaemia; 94% of infants (body weight under, 10 kg.), 87% of pre-school-children (weight 10 to 20 kg.), and 62% of school-children had a haemoglobin value of less than 12 g. per 100 ml. Parasitic infestation was very -common, about 50% of the children having positive blood slides for malaria, about 30% hookworm, and 30% urinary schistosomiasis. The degree of anaemia was assessed in comparable groups of children with and without parasitic infestation. Malaria appeared to reduce the haemoglobin concentration by about 1 to 1.5 g. per 100 ml., but there was no evidence that the presence of parasites was a major factor in the actiology of the anaemia. Coupled with a low dietary intake of iron and protein, however, it is considered that the presence of parasites may well aggravate the anaemia. Total and fractional plasma protein values were essentially normal in the 200 children in whom they were measured. There was a widespread deficiency of vitamin A, but there was no correlation between the haemoglobin concentration and the amount of vitamin A or carotene in the plasma. W. H. Horner Andrews

Allergy

600. Serological Evaluation of Immune Responses to Repository Injection of Ragweed Emulsion

H. FRIEDMAN, J. SPIEGELMAN, G. BLUMSTEIN, M. GERSHENFELD, and A. FISHMAN. Annals of Allergy [Ann. Allergy] 19, 991–1003, Sept., 1961. 5 figs., 35 refs.

In an investigation at Albert Einstein Medical Center, Philadelphia, Pennsylvania, 39 patients with ragweed hay-fever, most of whom had had previous hyposensitizing treatment, received one injection of water-in-oil emulsion of ragweed extract containing 50 to 100 times the maximum aqueous dose previously used. Of the 39 patients, "good" results were obtained in 34. Haemagglutination studies on samples of serum by the tannic acid and bis-diazotized benzidine methods showed a rise in titre in most cases after treatment. However, there was no correlation between the results of the two methods or between the clinical results and the haemagglutination titres, patients with excellent clinical results often showing hardly any rise in titre, and vice versa.

H. Herxheimer

601. The Incidence of Positive Intradermal Reactions and the Demonstration of Skin Sensitizing Antibody to Extracts of Ragweed and Dust in Humans without History of Rhinitis or Asthma

J. H. LINDBLAD and R. S. FARR. Journal of Allergy [J. Allergy] 32, 392-401, Sept.-Oct., 1961. 15 refs.

In 100 subjects without any history of nasal or respiratory allergy intradermal skin tests were carried out with various kinds of pollen extract, mould spores, and dust.

Even with an amount as small as 0.001 mg. N per ml. positive reactions were obtained in 5 subjects. With a tenfold amount a positive reaction occurred in 34 tests. In 8 of these subjects passive transfer tests were carried out and were positive in 5 of them. It is estimated that some 10% of these entirely asymptomatic subjects had skin sensitizing antibody in their serum. Some of the subjects, however, were over 40 years of age, and the authors point out that a positive result of a skin test is therefore not necessarily a sign of previous or future clinical allergic disease.

H. Herxheimer

602. Adverse Reactions to Injected Emulsified Pollen Extract in Allergic Patients on the West Coast: Relationship to the Total Dosage of Antigen

B. C. EISENBERG and W. R. MACLAREN. Journal of Allergy [J. Allergy] 32, 373-380, Sept.-Oct., 1961. 12 refs.

At Los Angeles County General Hospital 850 patients suffering from allergy to various pollens, house dust, or mould spores received injections of emulsified extracts of their specific allergen 3 or 4 times per year. The amount of allergen injected varied from 250 to 7,500

protein-nitrogen units. Adverse reactions occurred at first in about 5% but later, when mechanically prepared emulsions were used, in just over 2%. The authors state that there is an increased risk of adverse reactions in patients with strongly positive skin reactions, and the maximum of protein-nitrogen units given in one injection should [at least in the west coast region of the U.S.A.] not exceed 5,000.

Whether this treatment is as effective as the multipleinjection technique [so far as the latter is effective at all] the authors are not prepared to decide after only one year's observation.

H. Herxhelmer

603. A New Test for Detecting Anaphylactic Sensitivity: the Basonhil Reaction

W. B. SHELLEY and L. JUHLIN. *Nature* [Nature (Lond.)] **191**, 1056–1058, Sept. 9, 1961. 1 fig., 3 refs.

In a search for a safe and reliable predictive test for the detection of persons likely to be anaphylactic reactors the authors have developed, at the University of Pennsylvania School of Medicine, Philadelphia, a miniature anaphylaxis system in vitro consisting of the humanbasophil granulocyte, blood, and an antigen. To confirm the reliability of the test, samples of venous blood-(0.25 ml.) from 20 penicillin-sensitive and 20 nonsensitive patients were mixed with small quantities of penicillin or appropriate antigen in a concentration of 10⁻³ in physiological saline solution. After standing at room temperature for 15 minutes, 0·1-ml. samples were withdrawn and added to an ice-cold fixative composed of ethanol, chloroform, and acetone. After overnight fixation the cells were re-suspended and aliquots were filtered through a cellulose membrane filter, the latter being then selectively stained with toluidine blue, dehydrated, and cleared. After mounting, the basophil cells were counted and classified into categories on the basis of size, staining properties, number, and location of the basophilic granules. The technique enabled cells depleted of histamine to be distinguished from intact cells. For a test to be regarded as positive the authors suggest that at least half the basophils exposed to the test antigen should show evidence of degranulation. The results of the test correlated well with the clinical histories of individuals who had experienced anaphylaxis of different types.

It is pointed out that the test gauges the critical potential for anaphylaxis by determining the degree of anaphylactic sensitivity. But negative data obtained by this test reflect the patient's status only at the time of testing, so it is not an absolute test. Furthermore, the test antigen employed must not be a liberator of histamine per se and of course must not be used in concentrations high enough to remove granules from the basophil granulocytes of control patients.

G. B. West

Nutrition and Metabolism

604. Assessment of the Radiotriolein Test in Steatorrhoea

A. G. Cox. British Medical Journal [Brit. med. J.] 2, 933-938, Oct. 7, 1961. 3 figs., 41 refs.

There appear to have been few reported investigations designed to assess the reliability of the radiotriolein test, in which the excretion of triolein labelled with radioactive iodine is determined in the diagnosis of steatorrhoea. At the Royal Infirmary, Sheffield, therefore, the author, following the method of Lubran and Pearson (J. clin. Path., 1958, 11, 165; Abstr. Wid Med., 1958, 24, 242) has performed the ¹³¹I-triolein excretion test and concurrently measured the daily faecal fat excretion in 100 medical and surgical patients, of whom 33 had steatorrhoea and 67 had not, the criterion for steatorrhoea being a faecal-fat excretion of 7 g, or more per day.

In only 2 of the 67 patients without steatorrhoea was faecal excretion of ¹³¹I-triolein greater than 5% of the administered dose (this level being taken as the upper limit of normal). Of the 33 patients with steatorrhoea this value was greater than 5% in only 15, the results in the remaining 18 being considered to be "false negatives". Errors in stool collection could have accounted for only 2 false negatives; no explanation was found for the other discrepancies. In concluding that the ¹³¹I-triolein test is unreliable in the diagnosis of steatorrhoea the author compares his results with those of others and discusses at length theoretical aspects and several possible defects of the test.

M. Lubran

605. Serum Globúlin Deficiencies in Non-tropical Sprue, with Report of Two Cases of Acquired Agammaglobulinemia

K. A. HUIZENGA, E. E. WOLLAEGER, P. A. GREEN, and B. F. McKenzie. American Journal of Medicine [Amer. J. Med.] 31, 572-580, Oct., 1961. 1.fig., 37 refs.

This paper from the Mayo Clinic, Rochester, Minnesota, describes the occurrence of agammaglobulinaemia in 2 cases of non-tropical sprue or idiopathic steatorrhoea in which there was evidence of malabsorption. A series of 178 determinations on 103 patients with idiopathic steatorrhoea-had shown a fall in the serum albumin or globulin level or both, and electrophoresis of serum proteins in 20 further cases revealed a deficiency in the y-globulin fraction in 9. Agammaglobulinaemia associated with a sprue-like syndrome has not generally been attributed to the absorptive defect, apparently because of the expectation that defects in absorption would lead to deficiencies in the other protein fractions, particularly albumin, whereas only the serum γ -globulin fraction appeared to be reduced in these cases. Another reason is that the symptoms of agammaglobulinaemia appeared to precede those of sprue, though this has in fact been true in only about one-half of the cases reported in the literature and the evidence on which this is based is of questionable reliability. The authors suggest that in patients with sprue an absorptive defect may have been present for many years before the onset of symptoms and may even have existed from the time of birth.

Agammaglobulinaemia could either result from an inadequate supply of protein or other nutrients or be due to gastro-intestinal loss. With regard to the former, most experiments suggest that lack of protein is the most important factor, but it has also been shown that a deficient calorie supply can be a cause. Vitamins, in particular pantothenic acid and pyridoxine, are not important in man. Protein loss into the small intestine was considered in the authors' first case, but was excluded in view of the normal half-life of radioiodinated y globulin. [This does not in fact exclude the possibility of gastro-intestinal protein loss (see Jeejeebhoy and Coghill, Gut, 1961, 2, 123; Abstr. Wld Med., 1961, 30, 453).]

It was noted that in both cases correction of the malabsorption resulted in a rise in serum γ -globulin level, from zero to 0.28 g. per 100 ml. in Case 1 and from 0.8 to 1.5 g. per 100 ml. in Case 2. The authors present this as evidence that malabsorption is a factor in the production of agammaglobulinaemia and that it may be wholly responsible for the disease in some cases.

J. S. Malpas

606. Dietary and Biochemical Control of Phenylketonuria

F. S. W. BRIMBLECOMBE, J. D. BLAINEY, M. E. R. STONEMAN, and B. S. B. WOOD. *British Medical Journal [Brit. med. J.*] 2, 793–798, Sept. 23, 1961. 2 figs., 20 refs.

There is now evidence that restriction of phenylalanine intake begun in the early weeks of life can prevent the subsequent appearance of mental deficiency in infants with phenylketonuria. This paper from the Royal Devon Hospital and the Children's Hospital, Birmingham, describes the methods for identification of children suffering from phenylketonuria and its dietary control. Most of these patients require limitation of the intake of phenylalanine to between 10 and 30 mg. per kg. body weight per day, and an appendix to the paper gives the phenylalanine content of a large number and variety of foodstuffs. The calorie intakes recommended are 12% higher than for the normal child of equivalent age and the importance of the fat content of the diet is discussed. The urine becomes free from phenylpyruvic acid when the plasma level is 8 to 12 mg, per 100 ml., but the estimated optimum plasma levels are much lower than this. It is pointed out that excessive restriction of phenylalanine intake may lead to subnormal levels in the plasma with consequent loss of weight, vomiting; listlessness, and a generalized eczematous rash. Repeated estimations of plasma phenylalanine levels at regular intervals are necessary since the requirements of this amino-acid vary with different stages of development and at different ages. Winston Turner

Gastroenterology

607. Changes in the Sense of Taste in Patients with Cancer. (Изменения вкусовой чувствительности у больных раком)

I. Т. Abasov. Советская Медицина [Sovetsk. Med.] 25, 47-52, Sept., 1961. 1 fig., 3 refs.

In this investigation the author has assessed the sensitivity of the taste sense in normal subjects, in patients who had undergone radical gastrectomy for cancer at least a year previously, and in 250 patients suffering from cancer at various sites. For the test, graduated concentrations of quinine, hydrochloric acid, common salt, and glucose were applied with a pipette to the parts of the tongue most sensitive to the respective stimuli, the lowest concentration which produced the required sensation being noted and used as an index.

There was little or no difference in the sensitivity to any of these substances between the 30 normal subjects and the 14 gastrectomized patients, but in many of the 250 patients with unoperated cancer there was a marked decrease in sensitivity to quinine and glucose, while a slight decrease in that to salt was noted in patients with cancer of the gastro-intestinal tract, lungs and uterus; there was no appreciable change in the response to hydrochloric acid. Pyrexia and severe pain were both found to be associated with diminished taste sensitivity. In 3 of the patients there was perversion of the taste sense, a bitter taste, for example, being interpreted as acid or salt.

608. The Sense of Taste in Certain Gastric Diseases. (Состояние вкусового анализатора при некоторых заболеваниях желудка)

А. N. Demčenko. Советская Медицина [Sovetsk. Med.] 25, 52-55, Sept., 1961. 3 figs., 9 refs.

The author has investigated the taste sensitivity of 64 patients suffering from gastric disorders of whom 22 had functional dyspepsia, 24 chronic gastritis, and 18 peptic ulcer (3 gastric and 15 duodenal); a group of 16 healthy subjects served as controls. The method employed was similar to that of Abasov [see Abstract 607] except that the range of concentration of hydrochloric acid started at a higher level (0.05% instead of 0.006%).

The 22 patients with functional dyspepsia showed increased sensitivity to acid and sweet stimuli, whereas the response to salt and quinine was within normal limits. Successful treatment resulted in the restoration of sensitivity to normal. All the patients with chronic gastritis showed a lowered sensitivity to sweet, salt, and bitter stimuli, while by their response to acid they could be divided into two groups, those with hyperchlorhydria being more sensitive to acid than normal and those with hypochlorhydria less sensitive. These changes were permanent, and did not disappear under treatment. The 18 patients with peptic ulcer also showed a well-defined separation into two groups according to their sensitivity

to salt and acid stimuli, those with evidence of vegetative nervous disturbances and the pain syndrome showing increased sensitivity, while those whose symptoms were primarily dyspeptic were less sensitive than normal. These changes, too, tended to be permanent, although in a few cases there was some_diminution in hypersensitivity after treatment.

It appears that changes in motor and secretory activity as well as those in the trophic and vascular reactions of the gastric mucosa are associated with changes in sensitivity to acid, not only in the stomach but also in the mouth and in the taste buds, and that there is a corticovisceral basis for these gastric disorders.

L. Firman-Edwards

STOMACH AND DUODENUM

609. The Dumping Syndrome: an Investigation and a Cause

H. T. Cox and W. R. Allan. Lançet [Lancet] 2, 672-674, Sept. 23, 1961. 1 fig., 2 refs.

Investigations were carried out at Withington Hospital, Manchester, on 6 patients who had developed the dumping syndrome after gastrectomy (3 with additional vagotomy) to determine how far vascular dilatation is associated with this phenomenon. An egg—milk mixture with or without sugar at temperatures ranging from 98 to 135° F. (36·7° to 57·2° C.) was given to induce the dumping syndrome. There was no alteration in the haematocrit reading at the onset of dumping. In the recumbent position there was a slight rise in the pulse rate and also in the blood pressure, but in the standing position there was a marked rise in pulse rate and fall in blood pressure in every case.

Another series of investigations were carried out, first on 12 control subjects (7 patients awaiting gastrectomy and 5 who had undergone cholecystectomy) and then on 27 patients who had undergone various gastric operations without developing the dumping syndrome. Plethysmograph records were taken from the second toe before and after consumption of the egg-milk mixture. In the control subjects no change occurred in the recordings during 30 minutes. In the patients, in the recumbent position, all 27 recordings showed considerable peripheral vasodilatation. In the erect position (10 patients only) the recordings showed complete absence of vasoconstriction in 7 cases, slight vasoconstriction in 2, and further vasodilatation in one. A similar study was carried out on 3 patients with the dumping syndrome. In each case the plethysmograph showed considerable vasodilatation with the patient lying and no vasoconstriction with the patient standing. Further studies showed that the degree of peripheral vasodilatation produced by the egg-milk mixture after gastric surgery is comparable to the maximum reflex peripheral vasodilatation produced in a normal subject by external heat.

The authors discuss the implications of their findings and conclude that the dumping attack is "a form of postural hypotension which is usually associated in variable degree with alimentary symptoms".

[This paper should be read in full by those interested.]

B. F. Swynnerton

610. Gastric Ulcer in Hiatal Hernia

S. F. Ochsner. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 892-895, Sept. 30, 1961. 3 figs., 18 refs.

In 17 years 230,000 patients have been admitted to the Ochsner Clinic, New Orleans, Louisiana, among whom 490 had benign gastric ulcer and 1,212 hiatal hernia. Excluding cases of the Barrett type with a "gastric ulcer in the oesophagus", a gastric ulcer in the hernia was proved [? operatively] in 9 women and 6 men ranging in age from 30 to 85, and these form the basis of the present report. Of the 14 patients who had preoperative barium-meal examination, the ulcer was detected in 9; and of 8 patients subjected to gastroscopy, it was seen in 6. Medical treatment was apparently tried, but a "flexible therapeutic approach to fit specific requirements" is recommended. No results or details of the length of follow-up are given. It is suggested that. radiological examination would be more successful in detecting the presence of an ulcer if greater care were taken in filming a hiatal hernia. Denys Jennings

LIVER AND GALL-BLADDER

611. Experience with Portacaval Shunt for Portal Hypertension

G. E. Wantz and M. A. Payne. New England Journal of Medicine [New Engl. J. Med.] 265, 721-728, Oct. 12, 1961. 1 fig., 2 refs.

The authors report their experience with portacaval anastomosis at the New York Hospital-Cornell Medical Center, New York, based on 131 such operations, in 98 of which end-to-side and in 33 side-to-side anastomosis was performed. There were 25 postoperative deaths and a further 5 patients were lost to follow-up. In all but 3 of the cases the obstruction was intrahepatic, due to some form of cirrhosis. Haemorrhage from oesophageal varices was the indication for surgery in 120 cases. Some of the operations were performed as emergency treatment for bleeding varices and in goodrisk cases the mortality was no greater than in the elective operations. The shunts prevented further haemorrhage in only 2 out of 6 patients in whom mural thrombi were found in the portal vein at operation. In all the other successful cases, however, further haemorrhages were prevented, ascites was relieved, and hypersplenism reversed. Portal hypertension récurred in 7 patients and in 5 of these the recurrence was due to occlusion of the inferior vena cava by tumour or fibrosis. Dependent oedema, usually due to hypoalbuminaemia, occurred postoperatively in 42 patients, most of whom had had

ascites before operation. Postoperative encephalopathy was a troublesome complication in 22% of all patients surviving operation.

Patients were classified into "good-risk" and "badrisk" cases (by defined criteria) according to their preoperative hepatic reserve. In the good-risk cases the postoperative mortality was 7.5%; postoperative encephalopathy occurred in 10% of these patients, but was usually mild and transient, and 90% of the survivors lived for more than 3 years. In the bad-risk cases the postoperative mortality was 47.4%, 60% of the survivors had troublesome encephalopathy, and only 16.6% lived for more than 3 years.

P. C. Reynell

612. Acute Fatty Metamorphosis of the Liver

M. GOLDBERG and C. M. THOMPSON. Annals of Internal Medicine [Ann. intern. Med.] 55, 416-432, Sept., 1961. 9 figs., 32 refs.

In this report from the Philadelphia General Hospital and the Hahnemann Medical College and Hospital, Philadelphia, the authors present a clinico-pathological analysis of 40 histologically proven cases of fatty liver seen in the years 1938–58, excluding cases where specific hepatotoxins could have been implicated. Liver sections were graded into 5 groups according to the severity of fatty change and again into 5 groups according to the degree of fibrosis. Cases with 3+ or 4+ fatty change and 0, 1+, or 2+ fibrosis were classified as "fatty metamorphosis" (Group I) (29 cases). Those with 3+ or 4+ fatty changes and 3+ or 4+ fibrosis were classified as "fatty cirrhosis" (Group II) (11 cases). In 25 cases sections of liver were obtained at necropsy and in 15 by biopsy.

In all cases in which an accurate history was available there was evidence of excessive alcoholic intake, with a recent accentuation of intake in many, associated with a grossly inadequate diet. In patients in Group I there was often hepatic tenderness with accompanying abdominal pain. Jaundice was more common in Group II. but was seen in one-half of the whole series. Psychotic reactions were also common and hepatomegaly was present in nearly all patients. In 26 cases the patient died after a fulminating clinical course, half of them in hepatic coma. The diagnosis made by the clinicians concerned included Laennec's cirrhosis, cholecystitis, and acute hepatitis, and in only 4 patients was a fatty liver alone considered to be a diagnostic possibility. Laboratory data showed the frequent association of anaemia and leucocytosis. The results of liver function tests, though commonly abnormal in both groups, were more severely abnormal in Group II. In 6 patients the raised serum bilirubin content was accompanied by raised serum alkaline-phosphatase and cholesterol levels, suggesting obstructive jaundice. Treatment, mainly by feeding an adequate diet with vitamin supplements and bed rest, resulted in decreasing jaundice, loss of liver tenderness, and decrease in liver size. Patients in Group II often showed persistent abnormalities after clinical remission. Recurrent bouts of acute fatty infiltration of the liver may result in the production of cirrhosis or may occur in an already established alcoholic cirrhosis.

The authors discuss the experimental production of the fatty liver and the clinical features accompanying it in their patients. They also discuss the importance of fat embolism in producing dyspnoea and sudden death, this probably being the cause of death in 9 of their cases (7 in Group I, 2 in Group II).

A. E. Read

613. Non-esterified Fatty Acids and Lipoprotein Lipase Activity in Patients with Cirrhosis of the Liver

C. Chlouverakis and P. Harris. Gut [Gut] 2, 233-239, Sept., 1961. 5 figs., 28 refs.

At the Queen Elizabeth Hospital, Birmingham, the - authors have observed the lipolytic effect of intravenous heparin in vivo by measuring the plasma concentrations of non-esterified fatty acids before and after the administration of heparin in 11 normal subjects, 12 with cirrhosis, 3 with nephrosis, and 2 with diabetes mellitus. Measurements were also made of endogenous lipolytic activity in the plasma of 5 cirrhotic and 4 normal subjects in vitro. To study the effect of heparin in vivo 2 samples of arterial blood were first taken; 100 mg. of heparin was then injected intravenously and subsequent samples of arterial blood were obtained after 15, 30, 60, and 90 minutes for the estimation of non-esterified fatty acids. Observations were made on some subjects both after 12 hours' starvation and 3 hours after a fatty meal. The endogenous lipolytic activity of plasma was estimated by measuring the concentration of non-esterified fatty acids liberated by the action of samples of plasma on various emulsions of cocoanut oil for 2 hours at 37° C.

In the fasting state heparin caused a rise in the plasma non-esterified fatty acid level in the normal, diabetic, and nephrotic subjects, but not in those with portal cirrhosis, in whom the initial plasma levels were usually elevated (normal mean 712 μ Eq. per litre, S.D. 134; cirrhotic mean 1,470 μ Eq. per litre, S.D. 312). During alimentary lipaemia heparin induced a rise in the level of non-esterified fatty acids in the plasma of 3 normal and 2 nephrotic subjects tested. The average of the maximum rise was 1,804 μ Eq. per litre. Of the 4 subjects with portal cirrhosis similarly tested, 2 showed a normal rise, one a slight rise, and one a fall. Tests for endogenous lipolytic activity of plasma in vitro in the normal subjects gave negative results, whereas 4 of the 5 with portal cirrhosis showed substantial activity.

The lack of response to heparin in the fasting cirrhotic subjects does not appear to be dependent on hypoalbuminaemia, since in 2 patients the serum albumin value had been previously restored to normal by albumin infusions and the nephrotic patient with a low serum albumin level responded normally. It is also unlikely that the initial high levels of plasma non-esterified fatty acids in the cirrhotic patients were responsible, since the diabetic subjects had high initial levels and yet responded normally.

The high concentration of plasma non-esterified fatty acids in portal cirrhosis might be due to the increased endogenous lipolytic activity in the plasma of these patients, resulting from impaired inactivation of lipoprotein lipase by the liver. The authors consider that

the lack of effect of heparin in fasting cirrhotic subjects is due partly to exhaustion of the stores of lipolytic apoenzyme in the tissues and partly to a deficiency of plasma lipid substrate.

Hewett A. Ellis

614. Two Varieties of Haemolytic Anaemia in the Course of Cirrhosis of the Liver. (Deux variétés d'anémie hémolytique au cours de la cirrhose)

L, ZIEVE and E. HILL. Revue internationale d'hépatologie [Rev. int. Hépat.] 11, 385-408, 1961. 9 refs.

At the Veterans Administration Hospital (University of Minnesota), Minneapolis, the authors have studied 50 cases of haemolytic anaemia associated with cirrhosis of the liver seen during the course of 2 years. These cases could be divided into a hypersplenic variety, characterized by splenomegaly, and a hyperlipaemic variety, characterized by no enlargement of the spleen, but an increase in the serum lipid content. It was found that there was a severe degree of haemolysis in the hypersplenic group, this being associated with some moderate impairment of hepatic function. On the other hand, in the hyperlipaemic group the amount of liver damage was minimal and the episodes of haemolysis were brief.

In patients with the hypersplenic type studies with radioactive chromium revealed that there was destruction of erythrocytes in the spleen, and in some selected cases splenectomy was effective in reducing the degree of haemolysis. Liver biopsy examination, performed in 22 cases of the hypersplenic variety and in 21 of the hyperlipaemic variety, showed that the fatty infiltration was much more prominent in the latter group. A persistent low grade fever was common in both groups.

I. McLean Baird

615. Auto-immunization and Liver Cirrhosis
W. Mori and T. SuZuta. Nature [Nature (Lond.)] 192, 41-42, Oct. 7, 1961. 5 refs.

This post-mortem study was carried out at the University of Tokyo on 15 Japanese males ranging in age from 8 to 74 years. At necropsy, which was usually performed within 4 hours of death, liver tissue and blood were removed. Nearly all the specimens of liver showed some alteration in hepatic histology, though in most the primary disease process was not hepatic. Some of the removed liver tissue was then homogenized with saline solution, sodium azide added as a preservative and, after centrifuging, the supernatant fluid was removed for the serological test. Serum, also preserved with sodium azide, was incubated at 56° C. for 30 minutes before being used. In testing for auto-antibodies Ouchterlony's agar reaction method, as modified by Wilson and Pringle (J. Immunol., 1954, 73, 232), was used.

Of the 15 specimens, 2 showed a positive reaction, one after 4 days' incubation at 38° C. and the other only after 10 days' incubation. In both these cases the liver was cirrhotic, but negative reactions were obtained in another 4 cases of cirrhosis. The 2 positive cases had many similar histological features, including rather small, uniform pseudolobules surrounded by thin trabeculae of fibrous tissue. Portal lymphocytic infiltration and bile duct proliferation were slight. There was no nodular

hyperplasia or marked scarring. In both cases there was a history of alcoholism, and the cirrhosis was considered to be of nutritional origin; one of the 2 livers showed marked fatty metamorphosis. It is suggested that the release of fat droplets into the blood stream may be a possible cause of auto-immunization.

W. H. Horner Andrews

616. Loss of Life Due to Cirrhosis of the Liver: California

J. L. SCHWARTZ and W. R. LIPSCOMB. Journal of Chronic Diseases [J. chron. Dis.] 14, 386-395, Oct., 1961. 2 figs., 17. refs.

In the U.S.A. deaths from cirrhosis of the liver have increased in the last 30 years. In California in 1957 cirrhosis of the liver was the 8th main cause of death. Of those dying from cirrhosis, 72% were aged 35 to 64 years—in the most productive period of their lives. In the age group 45–54 the death rate from cirrhosis for both sexes was exceeded only by that from heart disease and malignant neoplasms. Cirrhosis is clearly one of the leading public health problems in California.

G. S. Crockett ..

617. Isotope Studies of the Development of Water and Electrolyte Disorders and Azotemia during the Treatment of Ascites

B. F. CLOWDUS II, W. H. J. SUMMERSKILL, T. H. CASEY, J. A. HIGGINS, and A. L. ORVIS. *Gastroenterology* [Gastroenterology] 41, 360-370, Oct., 1961. 7 figs., 41 refs.

In 14 patients with cirrhosis and ascites under treatment at the Mayo Clinic estimates were made at variable intervals before, during, and after diuresis of the amounts of exchangeable sodium, potassium and total body water, using the radioactive isotopes of these substances. Some patients became azotaemic, but these did not differ systematically in regard to the measured "spaces" from those without azotaemia. During treatment with diuretic drugs more sodium was lost than water, yet the serum sodium concentration increased, suggesting that sodium had come out of the cells. "Potassium depletion was not identified".

[This is a thorough study, but it perhaps indicates that "space" measurements without concurrent estimates of balance are an incomplete guide to changes in body fluids. Loss of sodium with an increase in the plasma sodium level would be consistent with repair of potassium depletion—which is very liable to occur in patients with cirrhosis treated by diuretics—but could well escape recognition by measurement only of exchangeable potassium.]

D. A. K. Black

618. Acute Alcoholic Hepatitis

A. G. BECKETT, A. V. LIVINGSTONE, and K. R. HILL. British Medical Journal [Brit. med. J.] 2, 1113-1119, Oct. 28, 1961. 4 figs., 41 refs.

The authors report in detail 7 cases of acute alcoholic hepatitis seen at the Royal Free Hospital, London, since 1953. Six of the patients were from the professional middle class, "a fact in keeping with the cost of alcoholic drinks in Britain". They were all drinking spirits

regularly, one bottle a day and often more at the time of onset, and most of them had been spirit drinkers previously. In 4 of the cases there had been previous attacks of jaundice. In only one case was there a history of deficient food intake. The most prominent symptom was anorexia, which had been present for a very variable time before the onset of the jaundice. Six of the patients complained of nausea and vomiting and 5 of them had severe epigastric pain. All the patients were febrile for at least 2 weeks after admission and in 5 of the cases this persisted for up to 4 weeks. This proved a useful distinguishing feature from other forms of hepatitis.

The results of liver function tests, while suggestive of liver cell damage rather than obstruction, were not disturbed in any consistent pattern, nor was the amount of abnormality in these tests proportionate to the severity of the patients' illness. The authors did not find that the leucocyte count was as useful a diagnostic aid as has been claimed by others. Six of the patients had some anaemia. The most useful diagnostic measure was needle biopsy, which showed the appearance of acute hepatocellular degeneration and fatty change proceeding to a patchy necrosis with some acute inflammatory reaction. These changes tended to subside after suitable treatment.

The treatment consisted in withdrawal of alcohol, bed rest, and treatment with a high-caloric carbohydrate diet. Where nausea and vomiting precluded oral feeding this was given as a continuous drip infusion of hypertonic glucose solution into the superior vena cava. Vitamin B was administered in large doses and in the presence of portal hypertension gut sterilization is recommended.

It is pointed out that the precise way in which an acute alcoholic debauch precipitates jaundice and a severe hepatitis such as described in these cases remains obscure, but that this condition should be distinguished from the jaundice occurring in the terminal phase of cirrhosis, which is irreversible, whereas acute alcoholic hepatitis may be associated with arrest and possibly recovery of the hepatic condition. The ultimate prognosis must, however, depend on the complete withdrawal of alcohol, which is the most difficult therapeutic step to achieve.

T. D. Kellock

619. Postalcoholic Hypoglycaemia and Toxic Hepatitis P. B. Neame and S. M. Joubert. *Lancet* [Lancet] 2, 893-897, Oct. 21, 1961. 18 refs.

The authors, working at the University of Natal and King Edward VIII Hospital, Durban, found that the most frequent cause of spontaneous hypoglycaemia in patients admitted in coma was post-alcoholic hypoglycaemia. In 10 months they saw 23 such cases, 21 in Africans and 2 in Indians, including a child of 5 who had accidentally taken alcohol. Six of these were chronic alcoholics and half were heavy week-end drinkers. All had been on a poor diet and most had not eaten for 12 to 24 hours before the drinking bout. Seven of the patients woke on the morning following their bout, but subsequently felt weak and lapsed into coma after a period of up to 2 hours, the interval between the end of the drinking bout and the onset of coma varying from 8 to 15 hours; these 7 patients had remained uncon-

scious for 8 to 11 hours before being seen. The remainder retired to bed intoxicated and were admitted in coma 12 to 24 hours later.

The blood sugar level on admission ranged from 9 to 47 mg. per 100 ml., the majority being in the region of 20 mg. per 100 ml. 'The hypoglycaemia was corrected by the intravenous administration of 20 to 70 ml. of 50% glucose solution; 18 recovered completely immediately, but the others remained mentally abnormal for periods up to 18 days, 2 (including the child) dying. The biochemical tests of liver function showed elevation of the serum glutamic-oxalacetic transaminase activity and very slight elevation of the serum bilirubin level, these returning to normal in the following days. Liver biopsy showed no evidence of acute disease other than absence of glycogen in the 3 cases examined on admission; in 3 cases changes typical of cirrhosis were seen.

It is concluded that the excessive drinking of alcohol causes a mild and transient hepatitis which is due to alcohol itself, and that the long-continued inadequate food intake makes the liver sensitive to it. Three factors are thought to contribute to the hypoglycaemia in these cases: (1) the period of inadequate food intake; (2) increased utilization of glycogen stores during the metabolism of alcohol; and (3) decreased glycogen synthesis during the utilization of these stores. The important factor was suggested to be a failure of gluconeogenesis resulting from the temporary dysfunction of the liver cells.

A. Gordon Beckett

INTESTINES

620. Observations on Secondary Malabsorption Syndromes of Intestinal Origin: Regional Enteritis, Lymphoma, Jejunal Diverticulosis, Gastrojejunocolic Fistula H. H. Scudamore. Annals of Internal Medicine [Ann. Intern. Med.] 55, 433-447, Sept., 1961. 5 figs., 42 refs.

This paper from the Mayo Clinic presents a comprehensive classification of the various types of the malabsorption syndrome on the basis of site of origin and mechanism of development, the four main groups being intestinal, gastric, pancreatic, and hepatobiliary. Some of the intestinal causes of secondary malabsorption are discussed in more detail. These include lymphoma, amyloidosis, scleroderma, radiation enteritis (in which malabsorption sometimes occurs), Whipple's disease (in which it always occurs), and regional enteritis, in which the incidence is variable. It is noted that in the last named the presence of abdominal pain, fever, tender abdominal masses, fistulae, or other evidence of chronic infection serves to distinguish it from non-tropical sprue.

The main symptoms and the physical and laboratory findings in 8 cases of regional enteritis giving rise to a malabsorption syndrome are analysed. Diarrhoea, loss of weight, and an abdominal mass occurred in nearly all patients, whilst steatornhoea, hypocalcaemia, and hypoalbuminaemia were the common signs. In 9 cases of lymphoma with the malabsorption syndrome the signs and symptoms were very similar to the above, except

that in addition there was a high incidence of perforation (4 cases) and haemorrhage (2 cases). Jejunal diverticulosis may give rise to steatorrhoea and a macrocytic anaemia, the latter being present in 3 of the 6 cases of this condition studied. The patients gave a history of intermittent diarrhoea and had symptoms suggestive of recurrent small-bowel obstruction. The periodic administration of broad-spectrum antibiotics to these patients, in addition to other dietary measures, is often beneficial. This was confirmed by studies of the absorption of vitamin B₁₂ labelled with radioactive cobalt and estimation of faecal nitrogen and faecal fat before and after treatment with neomycin and oxytetracycline. which showed that absorption of vitamin B₁₂, nitrogen. and fat was much improved. This contrasted with the results in patients with pernicious anaemia and healthy controls in whom no improvement occurred following antibiotic treatment, although in non-tropical sprue the absorption of labelled vitamin B₁₂ was helped. Finally, the author discusses 5 cases of gastro-jejuno-colic fistula. The main diagnostic features include prevalence in middle-aged men and in patients who have undergone gastroenterostomy, persistent diarrhoea, loss of weight, abdominal pain, and characteristic faeculent belching. All 5 of the author's patients developed a malabsorption syndrome. However, with surgical treatment the prognosis is stated to be excellent.

In general the prognosis of secondary malabsorption syndromes is not as favourable as that of the primary type. The author stresses the need, therefore, to confirm the diagnosis by radiological examination, examination of a peroral biopsy specimen of jejunal mucosa, or exploratory laparotomy. In the treatment of these secondary syndromes a gluten-free diet is seldom helpful; but correction of deficiency states is most important, together with the administration of steroids, radiotherapy, and surgery where appropriate.

J. S. Malpas

621. Distribution of Malignancy in Ulcerative Colitis N. P. G. Edling and O. Eklöf. Gastroenterology [Gastroenterology] 41, 465–466, Nov., 1961. 1 fig., 10 refs.

The distribution of 43 malignant tumors occurring in 41 patients with ulcerative colitis was recorded. It was found that these tumors tended to occur more frequently in the proximal than in the distal colon, in contrast to large bowel tumors in general.—[Authors' summary.]

622. The Value of Rectal Biopsy in the Diagnosis of Ulcerative Colitis

S. G. F. MATTS. Quarterly Journal of Medicine [Quart. J. Med.] 30, 393-407, Oct., 1961. 6 figs., 27 refs.

Specimens of rectal lining were obtained safely from 126 out-patients with ulcerative colitis at Southmead and Frenchay Hospitals, Bristol, and the Royal Hospital, Wolverhampton, with a modified Truelove suction biopsy apparatus, a modified "coldlite" type sigmoidoscope, and a special cautery. The earliest and mildest histological abnormalities seen consisted in an excessive infiltration of the mucosa with either round cells or poly-

morphonuclear leucocytes. Cases with gross sigmoidoscepic signs showed, in addition, histological evidence of superficial erosion, ulceration, or necrosis. Crypt abscesses were uncommon and were considered to be of dubious aetiological significance. Long-standing cases showed extensive round-cell infiltration of the mucosa and submucosa, often with some submucosal fibrosis. In healing or recently healed ulcerative colitis the rectal specimens often showed flattening or simplification of the epithelium.

Histological abnormalities can be expected in over 90% of cases of the disease. Although the histopathological changes are of a non-specific kind, biopsy is most helpful in quiescent cases in which sigmoidoscopic and other findings may be equivocal or normal. In such cases the epithelial cells may be normal or thin, the crypts fewer than normal and irregular in arrangement, and the goblet cells excessive in number.

A. Wynn'Williams

623. Dilatation of the Colon in Ulcerative Colitis P. A. SAMPSON and F. C. WALKER. *British Medical Journal [Brit. med. J.]* 2, 1119–1123, Oct. 28, 1961. 10 figs., 15 refs.

In this paper from the University of Birmingham the authors report 14 cases of acute toxic dilatation of the colon occurring in ulcerative colitis.

All 14 patients were subjected to primary colectomy. At operation perforation was found in 4 cases and 4 of the patients died after the operation. Two of the deaths were in patients with perforation before the operation and in the other 2 there was peritoneal contamination during the course of the operation when the friable, diseased colon was being removed. As far as could be judged from the serum potassium levels hypokalaemia did not appear to be the cause of the toxic dilatation, nor did destruction of the myenteric plexus, as has been suggested by others, for on histological examination of the resected specimens the ganglion cells were present in all and the most striking condition was degeneration of the muscle cells of the colon wall.

The authors draw attention to the extreme gravity of this condition and the importance which must be attached to dilatation of the colon even in patients in whom the disease may seem fallaciously to be improving as shown by a decrease in the number of bowel movements. They consider that primary colectomy is the only treatment which should be used in patients as gravely ill as these. The lesser measure of ileostomy is regarded as carrying too great a risk, as it is no protection against degeneration of the colon and further perforation.

T. D. Kellock

624. Circulating Antibodies to Milk Protein in Ulcerative Colitis

K. B. TAYLOR and S. C. TRUELOVE. British Medical Journal [Brit. med. J.] 2, 924-929, Oct. 7, 1961. 3 figs., 16 refs.

Following up the fact that some patients with ulcerative colitis improve when cow's milk is excluded from their diet, a study was undertaken at the Radcliffe Infirmary, Oxford, to determine whether antibodies to cow's milk

are present in the blood of patients with ulcerative colitis. In all, 75 patients and 50 normal persons were studied. The sera were tested against solutions of purified casein, lactalbumin, and lactoglobulin by the coated-tanned-erythrocyte test of Boyden as modified by Witebsky and Rose, the Ouchterlony gel-diffusion test and, in some cases, the passive cutaneous anaphylaxis test in guineapigs. Negative results were obtained in the last two tests.

The coated-tanned-erythrocyte test showed the presence of antibodies in some normal subjects and in some patients with ulcerative colitis. However, the proportion of subjects showing antibodies in high dilutions of serum was much higher in the ulcerative colitis group than in the control group. This was true for all three proteins, though the difference with lactalbumin did not quite reach conventional levels of statistical significance. There was some measure of association between the reactions to the different proteins, but this was not pronounced and a high level of reaction to one of them might coexist with negative reactions to the others. Analysis of the data in relation to various clinical features of the .75 patients with ulcerative colitis showed that the presence of high-titre reactions to milk proteins was not related to the age or sex of the patients studied, the type of diet, the activity or quiescence of the disease, the radiological extent of the disease, or corticosteroid therapy. The one feature in which there was some relationship was that for casein only there was a marked preponderance of high-titre reactions in patients with established, chronic disease.

It is considered likely that these serological reactions to milk are an indication of a more general disturbance of immunological responses and are not themselves the cause of the disease.

John Fry

625. Early Weaning in the Actiology of Ulcerative Colitis: a Study of Feeding in Infancy in Cases and Controls

E. D. ACHESON and S. C. TRUELOVE. British Medical Journal [Brit. med. J.] 2, 929-933, Oct. 7, 1961. 2 figs., 6 refs.

In an attempt to relate the aetiology of ulcerative colitis to some allergy to milk a study was made at the Radcliffe Infirmary, Oxford, of the feeding in infancy of 152 patients with classic ulcerative colitis. An equal number of control subjects, matched for age and sex, were also studied. The patients were all asked a standard series of questions by the same interviewer and in 74% of cases first-hand evidence was obtained from a parent or other relative by a postal questionary.

It was found that breast-feeding had not been established in 30.3% of patients with ulcerative colitis and in 14.7% of controls—a significant difference. The proportions weaned at the end of the first month were the same. Comparison of the two groups showed a consistently higher proportion of patients with ulcerative colitis who had been weaned in the first 2 weeks of life. It is concluded that it is very likely that early artificial feeding increases the liability to ulcerative colitis in later life.

John Fry

Cardiovascular System

626. Measurement of Arterial Ageing in Hypertensive Patients

- F. M. Abboud and J. H. Huston. Journal of Clinical Investigation [J. clin. Invest.] 40, 1915-1921, Oct., 1961. 2 figs., 17 refs.

The "arterial rigidity index" was estimated in 100 hypertensive out-patients at the Milwaukee County Hospital, Wisconsin: The method required the measurement of intra-arterial blood-pressure changes resulting from the inhalation of amyl nitrite before the onset of reflex tachycardia. "The ratio of the change in pulse pressure × 100 to the related decrease in diastolic pressure during this period is the index of arterial rigidity".

Rigidity indices were normal for age in 71 of the patients, while in 29 the indices were higher than normal. There were relatively more diabetics and patients with hypertension of more than 10 years' duration in the group with prematurely elevated indices. The number of females was also higher in this group, and Grade-III or Grade-IV eye-ground changes were more common. No difference was observed between the groups in regard to age, type of hypertension, incidence of left ventricular hypertrophy, and family history of hypertension or diabetes.

The authors state that there was no evidence to suggest that hypertension might have been caused by arteriosclerosis extending to the peripheral vascular system. If structural changes in the peripheral vascular bed play a major part in the aetiology of essential hypertension, they do not appear to be related to premature arterial ageing as determined by this test.

H. Caplan

627. Cardiac Output Measurement by External Countingof a Rapidly Excreted Indicator

W. H. Austin, J. W. Poppell, and R. J. Baliff. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 457-462, Oct., 1961. 14 refs.

The measurement of cardiac output by external precordial counting of intravenously injected radioactive isotopes has been shown to compare favourably with results obtained by the Fick method, but has certain drawbacks. Thus if isotopes with a long half-life are used the patient receives a large dose of radiation and also the persistence of this radiation complicates further similar measurements. On the other hand isotopes with a short half-life are impracticable since they decay rapidly and in many areas an adequate supply is not always available. For these reasons tracers which have a long half-life but which are rapidly excreted from the body would be ideal.

At the Sloan-Kettering Cancer Center, New York, the authors have investigated the value of "cholografin" labelled with radioactive iodine (131 I), of which 30 to $100\,\mu\text{c}$. was injected rapidly into an arm vein. Measurements were made over the fourth left rib at the sternal

border, using a collimator and a scintillation detector. Curves of the concentration of 131I were constructed and cardiac output assessed by the method summarized by Gorten and Stauffer (Amer. J. med. Sci., 1959, 238, 274). In all, 61 studies were made on 36 patients. By taking serial blood samples from 11 patients the mean half-time of ¹³¹I-labelled cholografin in the blood was fixed at 5.3 hours. Duplicate determinations of cardiac output in 8 patients by the method described showed a mean standard deviation of $\pm 3.9\%$, while in a further 8 patients in whom duplicate determinations were performed with ¹³¹I-labelled albumin the standard deviation was ±3.27%. A comparative study using both indicators in random sequence among 9 patients gave a standard deviation of $\pm 3.5\%$. These results compare favourably with those obtained with the direct Fick principle. D. Goldman

628. Differentiation of Massive Pericardial Effusion from Cardiac Dilatation Using I¹³¹ Albumin L. P. O'MEALLIE, W. D. LOVE, and G. E. BURCH.

L. P. O'MEALLIE, W. D. LOVE, and G. E. BURCH. American Heart Journal [Amer. Heart J.] 62, 453-456, Oct., 1961. 2 figs., 8 refs.

This paper from Tulane University, New Orleans. describes a technique that may help to differentiate cardiac dilatation from pericardial effusion. The dimensions of the heart shadow were first determined fluoroscopically; the intracardiac volume was then determined by measuring the radioactivity over the area of the cardiac shadow on a 4-point pattern after the intravenous injection of albumin labelled with radioactive iodine (radioactivity from the lungs and great vessels being shielded from the counter by lead). The intracardiac blood volume so determined was plotted against. the area of the precordium as monitored. Of 8 patients known to have pericardial effusion, 5 had a normal intracardiac blood volume and a large heart shadow. Of the other 3 patients, 2 were found at necropsy to have cardiac dilatation and a relatively small pericardial effusion; the third patient recovered, so that pathological confirmation of cardiac dilatation could not be obtained. It is claimed that these results indicate that this method offers a sound approach to the diagnosis of pericardial effusion and has the great merits of being simple and innocuous.

C. Bruce Perry

629. A Method of Treatment for Pericardial Pain A. S. Weissbein and F. N. Heller. Circulation [Circulation] 24, 607-612, Sept., 1961. 4 figs., 11 refs.

This paper from the 28th General Hospital of the U.S. Army Medical Corps describes the use of 15 ml. of 1% lidocaine (lignocaine) injected into the left stellate ganglion in the treatment of severe chest pain due to acute pericarditis in 2 patients. In one patient, who had suffered for 75 days, the pain was relieved within 15

minutes, but recurred 6 days later, responding again to a further injection. The second patient was treated on the 7th day of pain, which was relieved within 30 minutes and did not recur. The authors consider that the inferior cervical and first thoracic sympathetic ganglia may play a part in the transmission of this pain rather than the phrenic nerve.

I. Ansell

CONGENITAL HEART DISEASE

630. Clinical and Physiologic Changes following Surgical Closure of Atrial Septal Defect

J. Mortensen, L. G. Veasy, and A. F. Toronto. Diseases of the Chest [Dis. Chest] 40, 428-438, Oct., 1961. 5 figs.

Twenty-five consecutive patients with atrial septal defects have been carefully evaluated clinically and by cardiac catheterization both before and after surgical repair of the defect. Critical review of the data indicates that successful closure of an atrial septal defect results in prompt and significant improvement in symptoms, physical findings, objective laboratory tests, and cardiovascular dynamics. It appears that physiologic abnormalities return to normal or near normal promptly after the defect is closed. Thus, atrial septal defect appears to be a readily curable lesion.—[Authors' summary.]

631. Congenital Pulmonary Atresia with Intact Ventricular Septum. Clinicopathologic Correlation of Two

A. L. DAVIGNON, W. E. GREENWOLD, J. W. DUSHANE, and J. E. EDWARDS. American Heart Journal [Amer. Heart J.] 62, 591-602, Nov., 1961. 8 figs., 16 refs.

This paper is based on a study of the pathological findings in 20 hearts showing atresia of the pulmonary valve and an intact ventricular septum, which form part of the Mayo Clinic's collection of some 800 hearts; the paper also includes a retrospective analysis of the clinical findings and investigations carried out in the patients from whom the hearts were removed. In all the hearts there was complete obstruction at the pulmonary valve and also the pulmonary artery was smaller than the aorta, its diameter varying from about half that of the aorta to almost the same size. Otherwise, however, the hearts could be divided into two groups of markedly different structural type. In the first group there was a minute right ventricular chamber with a thickened wall, and the tricuspid valve, though small like the ventricle, was competent; these hearts also showed abnormal coronary anastomosis with large venous sinuses running into the ventricular chamber, while the right atrium was slightly enlarged. The second group was typified by incompetence of the tricuspid valve, and in 3 of the hearts an abnormal attachment of the valve as in Ebstein's deformity; the right atrium was very large.

In 6 cases with hearts of the first type the electrocardiogram (ECG) was available for study. In 4 of these it showed atrial enlargement and left ventricular dominance, the other 2 ECGs showing evidence of right ventricular overload and normal ventricular complexes.

For the second type of heart 4 ECGs were available, of which 3 showed atrial enlargement and right ventricular overload and the fourth also having fairly marked left ventricular R waves. The two types of heart could be even more clearly differentiated radiologically, the first group showing normal or only, slightly enlarged hearts with a hollow pulmonary conus and normal right border to the heart, while in the second group, in which there was tricuspid incompetence, the hearts were grossly enlarged with marked prominence of the right border. Of the 20 patients 16 had died under the age of 6 months, but there seemed to be no difference in the prognosis according to the type of heart. All had been cyanosed before the age of 48 hours, but the cyanosis was usually mild and could be relieved by oxygen. In 13 of the 16 cases a systolic murmur had been heard at the lower left sternal border, in 2 cases accompanied by a thrill.

The authors do not consider that the two types can be differentiated on clinical grounds, though they refer to the finding of a systolic thrill as possibly being evidence of a tricuspid incompetence. [Other signs of tricuspid incompetence, notably venous pulsation, are not mentioned, though terminal enlargement of the liver was noted.] The authors suggest that those cases in which there is a large right ventricle may be amenable to operation and that the possibility of differentiation, notably by radiological or electrocardiographic examination, into these two different groups is therefore of value.

H. G. Farquhar

VALVULAR DISEASE

632. The Production of Lactic Acid during Exercise in Normal Subjects and in Patients with Rheumatic Heart Disease

K. W. DONALD, J. GLOSTER, E. A. HARRIS, J. REEVES, and P. HARRIS. *American Heart Journal [Amer. Heart J.*] 2, 494-510, Oct., 1961. 7 figs., 20 refs.

A number of workers have shown that the concentration of lactic acid in capillary, arterial, and superficial venous blood following exercise is greater in patients with heart disease than in normal subjects. It has been assumed that this is due to the influence of lowered oxygen tension on the metabolism of exercising muscle, but lactic acid catabolism may also be impaired owing to the marked reduction in blood flow through other tissues. The purpose of the present study, reported from the University and Queen Elizabeth Hospital, Birmingham, was to investigate more precisely the relationship between the haemodynamic response to exercise and the production of lactic acid, the study including 7 normal subjects and 24 patients with rheumatic heart disease. mainly mitral stenosis, of varying severity. The exercise consisted in pedalling a bicycle ergometer for 10 minutes in the recumbent position, the rate of external work being maintained at a constant level. The brachial artery was cannulated in all'cases, and a cardiac catheter was placed with its tip in the pulmonary artery and a length of polythene tubing inserted into the femoral vein in 15 cases. The concentrations of lactic acid in arterial and venous blood were measured during the second 5 minutes of

exercise, while at the same time measurements of oxygen uptake and of oxygen saturation of arterial mixed venous and femoral venous blood were made.

These studies showed that the rise in oxygen uptake was very similar in normal subjects and in patients with mitral stenosis, but that the rise in lactic acid concentration in both arterial and venous blood was much greater in the patients with mitral stenosis. There was also a greater difference in femoral arterio-venous lactic acid levels in the patients and the femoral venous oxygen saturation fell to a lower level than in the normal subjects. A subsidiary study carried out on 41 patients at rest in bed showed that the concentration of lactic acid in arterial blood was similar in those who were severely disabled by heart disease and in patients without cardio-respiratory distress.

The authors then calculated the amount of lactic acid produced per ml. of oxygen used by the exercising legs and found that this amount increased considerably as the femoral venous saturation fell. By this means a correlation was established between the concentration of lactic acid in arterial blood, the femoral venous oxygen saturation, and the oxygen uptake, which held good both for normal subjects and cardiac patients. The amount of lactic acid produced by the exercising muscles can be estimated by first determining the blood flow through the leg during exercise. This value correlated well with the observed concentrations of lactic acid in arterial blood. The authors point out that it has now been shown that at rest the combustion of carbohydrate accounts for only a portion of the oxygen uptake of muscle, and hence it is unwise to draw any conclusions from calculations based upon the lactic acid production of muscle until all possible muscle metabolites have been studied simultaneously.

633. Mitral Valve Anatomy and Prosthetic Valve Design R. W. M. Frater. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 36, 582-592, Nov. 8, 1961. 4 figs., 5 refs.

G. Clayton

634. Clinical and Haemodynamic Observations on Combined Mitral and Aortic Stenosis

M. Honey. British Heart Journal [Brit. Heart J.] 23, 545-555, Sept., 1961. 4 figs., 18 refs.

This paper from Guy's Hospital, London, discusses the clinical and haemodynamic features in 35 patients with both mitral and aortic stenosis without dominant regurgitation at either valve. Most of the patients had symptoms of bronchitis, which are common in mitral stenosis, but they rarely complained of angina or syncope, although these symptoms are frequently seen in severe lone aortic stenosis. Electrocardiographic and radiological evidence of left ventricular hypertrophy was also slight in the patients with combined valvular disease. The author suggests that the main reason for the observed differences between the patients in this series and those with lone aortic stenosis was a low cardiac output when the mitral valve was severely stenosed. Using Gorlin's formula he shows, for example, that halving the cardiac

output in a patient with severe aortic stenosis can cause the systolic gradient across the valve to fall from 80 mm. to 20 mm. Hg. Clinically significant aortic stenosis may then be overlooked and the systolic murmur may be ascribed erroneously to mitral regurgitation.

C. T. Dollery

CORONARY DISEASE AND MYOCARDIAL INFARCTION

635. A Double-blind Study of Rescrpine in Angina Pectoris

B. A. ROSENBERG and M. MALACH. Diseases of the Chest [Dis. Chest] 40, 448-453, Oct., 1961.

Previous reports on the effect of reserpine in angina pectoris are open to criticism on the grounds of the absence of controls, brevity of trial, or infrequent use of the double-blind technique. In this study reported from the State University of New York Downstate Medical Center and Kings County Hospital Center, New York, 18 out-patients of average age 61 years and with an average duration of angina of 3 years were selected. They were given identical tablets of reserpine (0.1 mg. 4 times daily) or of placebo and reviewed every 2 or 3 weeks. After 6 months reserpine and placebo were interchanged, and the review continued for another 6 months. Thirteen of the 18 completed the course. The daily need for nitroglycerin and the effort tolerance were recorded and the patient was said to have "improved" if the former fell by a half or more, or if the latter rose by a half or more.

No significant difference was found between treated patients and those receiving the placebo at any stage during the treatment or at the end. Side-effects occurred similarly in treated and untreated patients with the exception of dizziness, which was reported more often with reserpine.

[A separate analysis of hypertensive patients with angina would be worth while.]

J. A. Cosh

[Although 30 references are cited in the text of this paper, no details of them are given, a footnote stating that "all references will appear in reprints". This is a pernicious practice which cannot be too strongly condemned.—EDITOR.]

636. Intermediate Coronary Syndrome

R. J. VAKIL. Circulation [Circulation] 24, 557-571, Sept., 1961. 12 figs., bibliography.

This paper from the King Edward Memorial and Bombay Hospitals, Bombay, describes the "intermediate coronary syndrome" in 251 cases seen in consultative practice. Most of the patients complained of "infarction-like" or "angina-like" pain of moderate severity lasting 15 minutes to 2 hours. There were only slight changes in pulse rate, blood pressure, or temperature and no evidence of shock, congestive failure, or gross myocardial necrosis. In the majority of cases the electrocardiogram showed ischaemic features, such as a depressed, "trough-like" S-T segment, isolated deep or shallow inversion of the T wave, or "coving" of the S-T segment with diphasic or inverted T wave. The

antero-lateral wall was affected more often than the posterior. The sequence of events, with return to normal, was much more rapid than in myocardial infarction, being a matter of hours or days rather than weeks or months. There was no involvement of the QRS complex or reciprocal changes in the ST-T segments. In 91 cases the patient developed acute myocardial infarction within 3 months of the initial attack of pain.

I. Ansell

637. Tobacco and Coronary Atherosclerosis. Study of 956 Cases and 956 Controls. (Tabac et athérosclerose coronarienne. Étude de 956 cas et 956 témoins)

D. SCHWARTZ, G. ANGUERA, and J. LENEGRE. Revue française d'études cliniques et biologiques [Rev. franç. Ét. clin. biol.] 6, 645-656, Aug.-Sept., 1961. 22 refs.

In this [well conducted] investigation carried out in the cardiae departments of the Hôpital Boucicaut and Hôpital Lariboisière, Paris, a smoker was defined as one who had smoked in the preceding 10 years an average of at least one cigarette or 1 g. of pipe tobacco per day. (As the proportion of subjects who smoked more than one cigar a day was less than 1 in 300 cigar smoking was not taken into consideration.)

A comparison of the smoking habits of 956 patients suffering from angina pectoris or myocardial infarction, or both, with those of 956" healthy" controls of similar sex and age drawn from the casualty departments showed that in the cardiac group male patients were heavier smokers and the incidence of inhalation was considerably higher. It was also found that the risk in smokers was nearly the same as in non-smokers so long as no inhalation took place, and that the risk increased with increasing smoking mainly because heavy smokers usually inhale more often; the differences in regard to inhalation were statistically highly significant. In patients with hypertension inhaling appeared to have little influence, but inhaling of the smoke was shown to be correlated with a gross increase in the incidence of obliterative atherosclerotic lesions in the lower limbs. The authors conclude that there is a causal relationship between inhalation and the incidence of atherosclerotic lesions and they suggest that the different results obtained in previous surveys may have been due to the fact that inhalation and smoking were not assessed separately.

Z. A. Leitner

638. A Clinical Study of Shock Occurring during Acute Myocardial Infarction. An Analysis of 58 Cases H. E. Heyer. American Heart Journal [Amer. Heart J.] 62, 436-446, Oct., 1961. 4 figs., 40 refs.

The author presents a clinical study of severe shock as seen in 58 out of 714 cases of acute myocardial infarction studied at the Southwestern Medical School of the University of Texas, Dallas, the incidence of shock in this series being thus about 8%. The criteria for the diagnosis of shock included: (1) definite clinical signs of shock such as sweating, weakness, pallor or cyanosis, absent or small pulse, moderate tachycardia, nausea, and often a dulled sensorium; and (2) a fall in the blood pressure to 80 mm. Hg systolic or below (or to 90 mm. Hg in previously hypertensive patients); hypotension

alone was not considered evidence of shock. In 62% of the patients shock appeared within 24 hours of the onset of the infarction and in 91% within 72 hours. Of these patients 29 (50%) died, 2 before therapy could be started, and 2 before adequate therapy could be given. The mortality for the whole series of 714 patients was 22.5%.

All the patients with shock were treated with vasoconstrictor agents, L-noradrenaline being the agent of choice, but in some patients mephentermine was given for varying periods before administration of adrenaline. The longest duration of treatment following which the patient survived was 1134 hours., The most important factor affecting prognosis was the duration of shock before treatment was begun; thus when therapy was started within 2 hours of the onset of shock the mortality was 40%, but when it was delayed for over 2 hours the mortality rose to 78%. No patient survived when treatment was delayed over 2½ hours. Other adverse factors were the development of arrhythmias, congestive heart failure, anuria, and lack of prompt response to vasopressor therapy. The rate of administration of the pressor agent required to achieve an effect was also of considerable prognostic value. The importance of early recognition and prompt treatment of shock in myocardial infarction is stressed. C. Bruce Perry

639. Disability Absenteeism of Industrial Workers with Myocardial Infarcts

N. K. Weaver. American Heart Journal [Amer. Heart J.] 62, 457-461, Oct., 1961. 7 refs.

This study, reported from Tulane University School of Medicine, New Orleans, deals with absenteeism due to disability among 100 subjects selected on the basis of an established diagnosis of healed myocardial infarction and who had been back at work (at an oil refinery) for at least one year. The average age of the subjects was 50 years, compared with 45 years for the entire worker population. Complete information as to absence from work and also the duration and cause of such absence was collected for each subject and compared with similar data for the whole refinery population. During the study 7 of the subjects became totally incapacitated and 3 died. The average period at work of these subjects after the initial episode of myocardial infarction was 4.7 (range 1 to 17) years; 10 of them developed a second infarct and 2 a third.

It was shown that for the subjects who had suffered infarction—the average period of absence from work annually was 10 days compared with an average of 9.9 days for all workers. The annual number of absences per employee was 1.2 for the infarction group and 1.1 for all workers. The average duration of absence (severity rate) was 8.3 days for the cardiac group and 8.9 for the whole worker population. Only 2.7 days out of the 10 days' absence each year of the cardiac workers were due to cardiovascular disease. The duration of absence of salaried employees (42 in number with a total of 210 man-years of work) averaged 6.7 days yearly, compared with 12.7 days lost by the wage earners (58 in all with a total of 260 man-years). There was no

significant difference in absenteeism as between different age groups in the cardiac group. Thus the absence from work of patients with healed myocardial infarction did not differ materially from that of the whole worker population.

C. Bruce Perry

640. Ventricular Premature Beats in the Diagnosis of Myocardial Infarction

A. BISTENI, G. A. MEDRANO, and D. SODI-PALLARES. British Heart Journal [Brit. Heart J.] 23, 521-532, Sept., 1961. 14 figs., 19 refs.

At the National Cardiological Institute of Mexico, Mexico City, an experimental and clinical study was carried out of the value of a ventricular premature beat (V.P.B.) in the diagnosis of myocardial infarction. In dogs with a normal heart, stimulus of the ventricle produced a V.P.B. with a bundle-branch-block pattern typical of the opposite ventricle. Only after myocardial infarction was produced by ligation of the anterior descending branch of the left coronary artery did a V.P.B. show a QR pattern in leads reflecting the potential change in the ventricle. Examination of the electrocardiograms obtained from the records of patients with 'myocardial infarction, proven at necropsy, sometimes allowed a correct diagnosis to be made from a V.P.B. which was not suggested by the sinus beats. In other instances both the V.P.B. and the sinus beats indicated an infarction.

The authors stress that infarction of the anterior part of the lower one-third of the septum can be recognized only in the presence of asynchronous ventricular activation because of the normal electrical preponderance of the free left ventricular wall.

C. T. Dollery

HEART FAILURE

641. Mechanisms of Hyponatremia in Chronic Congestive Heart Failure

T. TAKASU, N. LASKER, and R. J. SHALHOUB. Annals of Internal Medicine [Ann. intern. Med.] 55, 368-383, Sept., 1961. 7 figs., 41 refs.

Writing from Jersey City Medical Center, New Jersey, the authors describe in great detail an investigation of 18 oedematous patients with congestive cardiac failure accompanied by hyponatraemia, the initial plasma sodium levels ranging from 117 to 130 mEq. per litre. The study was divided into two parts, in both of which serial estimations were performed at 2- to 4-hourly intervals for 24 hours of the urinary and plasma concentrations of sodium and potassium, creatinine clearance, and urinary and plasma osmotic pressures, first after a water load of 15 ml. per kg. body weight and, in the second part of the test, after the patients had been kept without fluids for 36 hours.

To these procedures three different types of response were noted. (1) In 6 patients with mild oedema which was easily controlled with digitalis and/or salt restriction and diuretics a prompt diuresis occurred after the administration of water, this being associated with a slight fall in plasma osmotic pressure and a marked fall in

urinary osmotic pressure. The reverse changes were noted on dehydration, thus indicating a reduced but adequate ability to dilute and concentrate urine. Plasma sodium levels varied little and it is suggested that in these patients the osmo-receptors are "set" at a lower level. (2) In 9 patients with more marked oedema which was refractory to treatment there was a tendency to signs of water intoxication after the water loading test, and mild uraemia and hypokalaemia frequently developed. No water diuresis took place, and an inverse relationship between urinary and plasma osmotic pressures was noted, indicating an absence of antidiuretic hormone. (3) The third group consisted of 3 patients in whom there was a delayed water diuresis associated with a sudden increase in creatinine clearance and increased rates of urinary sodium and potassium excretion. Similarly, dehydration was followed by an increase in urinary osmotic pressures which reached their highest levels during the nocturnal increase in glomerular filtration rate.

From these results the authors conclude that hyponatraemia in congestive cardiac failure could result from one of the following mechanisms: (1) resetting of the osmoreceptors at a lower level; (2) glomerulo-tubular imbalance; (3) sustained secretion of antidiuretic hormone; or (4) a combination of glomerulo-tubular imbalance and a low setting of the osmo-receptors.

[This is an interesting paper which would repay reading, in full.]

H. F. Reichenfeld

642. Pathogenesis of Congestive Heart Failure: Effect of Posture and Exercise on Plasma Volume and Plasma Constituents

L. T. ISERI, E. L. BALATONY, J. R. EVANS, and M. G. CRANE. Annals of Internal Medicine [Ann. intern. Med.] 55, 384–394, Sept., 1961. 2 figs., 40 refs.

The effects of change in posture and light exercise on plasma volume and plasma constituents were studied in patients with various forms of mild heart disease. Serial plasma volumes were determined by following the changes in the plasma concentration of injected radio-iodinated serum albumin.

When the patients were made to stand from a recumbent position the plasma volume decreased and the hematocrit increased but the plasma osmol and sodium concentrations remained the same. No change in plasma volume occurred when patients were made to stand in deep water. These observations were interpreted to indicate transudation of plasma ultrafiltrate from the capillaries into the interstitial spaces because of increased hydrostatic intracapillary pressure.

When patients were made to exercise lightly on the treadmill or on the two-step platform the plasma volume decreased and the hematocrit, osmol, and sodium concentrations increased. Virtually no change occurred in the total plasma osmol or sodium content. It was felt that circulatory stress of exercise would cause an increase in osmotic pressure of the cells resulting in migration of water from the plasma compartment into the cells. These changes were considered to initiate active renal retention of salt and water in the pathogenesis of congestive heart failure.—[Authors' summary.]

Clinical Haematology

643. Ineffective Erythropolesis

F. I. HAURANI and L. M. TOCANTINS. American Journal of Medicine [Amer. J. Med.] 31, 519-531, Oct., 1961. 2 figs., bibliography.

The authors of this paper from the Jefferson Medical College, Philadelphia, have made a study of crythrokinetics in 37 subjects with various haematological disorders. The disorders included thalassemia, abnormal haemoglobins, myelosclerosis, myeloid leukaemia, aplastic anaemia, refractory normoblastic anaemia, haemochromatosis, and megaloblastic anaemia. Estimations were made of the serum iron level, the plasma iron turnover, the plasma iron clearance rate, and the radioactive iron utilization curve, and the blood volume was determined by means of crythrocytes labelled with radioactive chromium.

The authors use a new term—" ineffective erythropoiesis"—to describe a condition in which there is an increase in total erythrocyte production of great magnitude, but most of the synthesized heme is destroyed in situ and does not reach the peripheral circulation. In these circumstances there is an active, hyperplastic marrow and an increased plasma iron turnover with poor erythrocyte utilization of iron. The faecal urobilinogen content is significantly increased.

Ineffective erythropoiesis was found in thalassemia, refractory normoblastic anaemia, and megaloblastic anaemia. It was absent in the haemoglobinopathies, myeloid leukaemia, and aplastic anaemia, in addition to haemochromatosis. The limitations of these diagnostic tools are emphasized and it is recommended that in measuring erythropoiesis as many parameters as possible should be determined.

I. McLean Baird

644. Autoimmme Hemolytic Disease. Antibody Dissociation and Activity

R. S. EVANS, M. BÍNGHAM, and P. BOEHNI. Archives of Internal Medicine [Arch. intern. Med.] 108, 338-352, Sept., 1961. 1 fig., 15 refs.

At the University of Washington School of Medicine, Seattle, the authors have studied the rate of transfer in vitro, and the conditions for such transfer, of antibody from patients' erythrocytes to normal erythrocytes. Of 10 patients suffering from various types of autoimmune haemolytic disease it was possible in 6 of them to carry out serial observations of antibody transfer and to relate them to the patients' response to steroid therapy. In 3 of the 10 patients it was found that human serum had to be present for the transference of antibody to normal erythrocytes, but that in the remaining cases saline medium was sufficient. It was concluded that the rate of transfer of antibody from patients' to normal red cells is a reflection of the concentration of antibody on the cell surface, and that this is positively correlated with the severity of the haemolytic process. In several

cases it was possible to demonstrate that the administration of steroid drugs caused a reduction in the amount of antibody that could be transferred, a finding which is in agreement with the generally held view that steroids produce their beneficial effects by reducing the amount of autoantibody formed.

[This is an important paper which should be read by all those interested in autoimmune haemolytic disease and the antiglobulin reaction.]

J. V. Dacte

645. S-C Hemoglobin: a Clinical Study

G. L. RIVER, A. B. ROBBINS, and S. O. SCHWARTZ. Blood [Blood] 18, 385-416, Oct., 1961. 10 figs., bibliography.

The authors report from Northwestern University, Chicago, a clinical study of 75 patients with S-C haemoglobin disease, all but one of whom were negroes. Since, in the American negro, the incidence of S haemoglobin, that is, haemoglobin in which valine has been substituted for glutamic acid, ranges from 8 to 11% and the incidence of C haemoglobin, that is, haemoglobin in which lysine is substituted for glutamic acid, from 2 to 3%, this group of patients is remarkable for its size. Clinically, pain in the splenic area was the most common presenting symptom, splenomegaly being present in about two-thirds of the cases. Haematuria, epistaxis, and concomitant infections occurred frequently and were thought to be associated with the underlying S-C disease. All but 5 patients showed sickling of erythrocytes. The proportion of target cells varied from under one to over 80%. It is concluded that the diagnosis of this disorder must still rest on electrophoretic studies of the haemoglobin, although a number of clinical and haematological features, which are discussed, are suggestive.

Janet Vaughan

646. Red Cell Filtration and the Pathogenesis of Certain Hemolytic Anemias

J. H. Jandl, R. L. Simmons, and W. B. Castle. *Blood* [*Blood*] 18, 133-148, Aug. [received Oct.], 1961. 5 figs., 35 refs.

This paper from the Thorndike Memorial Laboratory, Harvard Medical School, reports critical observations on the rate and extent of passage of pathological or agglutinated human erythrocytes through artificial membrane ("millipore") filters. These consist of an inert chemical matrix which is penetrated by non-branching capillary tubes or pores $5\,\mu$ in diameter and orientated perpendicularly to the filter surface, thus providing an analogue (admittedly imperfect) of the capillary bed. The results obtained with this device brilliantly underline the importance of the filter-bed mechanism in relation to haemolysis in vivo. For example, sickle cells were selectively trapped under conditions of reduced oxygen tension and raising the filtration pressure did not increase

the number passing the filter. Cells agglutinated by anti-A were retained by the filter, but some were forced through if the pressure was raised. Erythrocytes coated with anti-D or incomplete autoantibody were retained by the filter only in the presence of rouleaux-producing agents such as polyvinylpyrrolidone (polyvidone) or fibrinogen and only at low pressures, and a small fraction of hyperspheroidal cells from several patients with hereditary spherocytosis were found to be retained by a single passage through the filter.

[This important paper should be read by all those interested in haemolytic mechanisms.] J. V. Dacie

647. Hemolysis in vitro and the Anemia of Leukemia W. H. Crosby, C. Vullo, and S. Garriga. Blood [Blood] 18, 220-224, Aug. [received Oct.], 1961. 1 fig., 4 refs.

In 1957 Crosby and Benjamin (Blood, 12 [not 7 as given], 701; Abstr. Wld Med., 1958, 23, 113) described an abnormal rate of autolysis in vitro of the blood of certain patients with leukaemia or other disseminated neoplasms. The haemolysis occurred when heparinized or defibrinated blood was incubated at 37° C. for more than 6 hours, and it differed from other known types of haemolysis in that calcium had to be present; reduction in the pH of the blood or the addition of an excess of glucose inhibited haemolysis. It was concluded that the accelerated haemolysis was the result of an abnormality of the plasma which permitted calcium to react harmfully on the erythrocytes.

The present paper from the Walter Reed Research Institute, Washington, D.C., deals primarily with the correlation between the results of the haemolysis test in vitro and evidence for haemolysis in vivo. No correlation could in fact be demonstrated, nor could the results of the test be correlated with the type of leukaemia or the occurrence of remission on treatment. The defibrinated-blood technique appeared to be more sensitive in demonstrating haemolysis than that using heparinized blood. Lysis was accelerated in 33 out of 44 cases of acute leukaemia and in some patients reversion of the rate of lysis to normal was the first sign of the beginning of a remission.

J. V. Dacie

648. Results of Treatment in 71 Patients with Idiopathic Thrombocytopenic Purpura

M. C. MEYERS. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 295-302, Sept., 1961. 1 fig., 10 refs.

This paper reviews the results of treatment of 71 adolescent and adult patients with idiopathic thrombocytopenic purpura studied at the Simpson Memorial Institute, University of Michigan, Ann Arbor, during the 11-year period 1950–61. All were treated with ACTH (corticotrophin) or corticosteroids, and those who relapsed on discontinuing treatment were re-treated and underwent splenectomy. In 31 cases restoration of a normal platelet count and control of bleeding were achieved by medical treatment and in 10 of these the remission has been sustained for periods of 10 months to 11 years. One patient who responded to ACTH had

an immediate splenectomy because of a history of chronic purpura. Twenty patients relapsed on cessation of treatment and splenectomy was carried out on 17 of these after a second or third remission had been induced. Normal platelet levels were achieved in 15. Splenectomy was also performed on 36 of 40 patients who had a suboptimal response to ACTH or corticosteroids, a sustained remission resulting in 30. Thus of 54 patients who underwent splenectomy, 46 had a sustained remission of thrombocytopenia. In all 10 patients who responded to medical therapy alone the purpura was of short duration and the response to treatment was optimal. Sustained remissions did not occur when the purpura was of more than 4 months' duration. Age and sex were found not to be of prognostic importance.

Eleven patients in the series died, 5 of them from unrelated conditions. Of the remainder, one patient proved to have Hodgkin's disease and another died of a post-operative infection. The rest died of haemorrhage, 2 preoperatively and 2 at intervals of 2 and 10 years respectively after splenectomy. Systemic lupus erythematosus occurred only in 2 patients and non-fatal postoperative infection in 3, in all of whom infection was easily controlled.

It is concluded that ACTH and corticosteroids are of great value in controlling bleeding before splenectomy, and that their use is not followed by severe or frequent postoperative infection. Splenectomy does not increase the liability to the development of systemic lupus erythematosus.

J. L. Markson

649. Increase in Cell Volume and Pulmonary Changes in Polycythaemia Vera. [In English]

T. THIEDE and E. CHIEVITZ. Acta medica Scandinavica [Acta med. scand.] 170, 443-448, Oct., 1961. 3 figs., 3 refs.

At the Finsen Institute, Copenhagen, between 1948 and 1960 the total circulating blood volume (T.C.B.V.) and the total circulating erythrocyte volume (T.C.E.V.) were measured in 119 patients with polycythaemia vera seen during that period, 78 of the patients being male and 41 female. The method employed was that of Bohr, using radioactive phosphorus. The normal range for T.C.B.V. is 50 to 80 ml. per kg. body weight and T.C.E.V. 29 ml. per kg.; values over 90 ml. and 35 ml. respectively per kg. were regarded as pathological.

No constant relationship between the T.C.B.V. and the haematocrit value was found, nor did the haemo-globin level give any firm indication of the T.C.B.V.; thus 50% of patients with a fiaemoglobin level of over 140% had a normal blood volume, while 30% of patients with a haemoglobin level of less than 120% had a T.C.B.V. over 90 ml. per kg. There was better correlation between the haemoglobin level and the T.C.E.V. Pulmonary changes were estimated by observing the density of the vascular markings and measuring the width of the pulmonary artery on chest radiographs. The severity of the pulmonary changes showed good correlation with increases in the T.C.B.V., and correlation was also good between the T.C.B.V. and the presence of hepatomegaly and, to a lesser extent, of splenomegaly.

The authors therefore conclude that it is important to regulate the treatment of polycythaemia vera by measurement of the total circulating blood volume since the haemoglobin and haematocrit values may be misleading.

M. C. G. Israëls

650. The Incidence of Carcinoma in Patients Dying from Leukaemia, Malignant Disorders of Plasma Cells, and Malignant Lymphoma

J. S. CORNES, T. G. JONES, and G. B. FISHER. British Journal of Cancer [Brit. J. Cancer] 15, 200-205, June [received Aug.], 1961. 10 refs.

The present study was prompted by the finding of 5 instances of carcinoma coexisting with malignant lymphoma of the large or small intestine in a series of 40, consecutive cases of the latter disease. This incidence of 12.5% was thought to be excessive. In a further study of 100 cases of benign lymphoma of the rectum there were 7 patients with carcinoma. The records of 14,944 consecutive necropsies performed at the Postgraduate Medical School of London and Westminister Medical School were then scrutinized. Amongst these were 588 cases of neoplasms of the reticulo-endothelial system made up of 265 cases of leukaemia, 43 cases of plasmacytoma, and 280 cases of malignant lymphoma. In these three sub-groups the incidence of coexisting carcinoma was 3.4%, 4.6%, and 2.1% respectively, a combined incidence of 2.7%. Amongst the 280 cases of malignant lymphoma in this larger series there was only one case in which the disease originated in the gastrointestinal tract. Within these broad groups of reticuloendothelial neoplasia there was no special tendency for carcinoma to be associated with particular varieties of disease. In 8 of 16 cases the diagnosis of carcinoma preceded the diagnosis of reticulo-endothelial neoplasm, in 5 cases, it followed, and in 3 cases the two diseases were diagnosed at the same time. No explanation can be offered for the very high incidence of carcinoma in cases of malignant lymphoma of the large or small intestine compared with the incidence of carcinoma in cases of malignant lymphoma in general. A. G. Balkie

651. Studies of Total-body Irradiation and Attempted Marrow Transplantation in Acute Leukemia. [In English] G. A. Andrews, B. W. Sitterson, A. L. Kretchmar, and R. Tanida. Acta haematologica [Acta haemat. (Basel)] 26, 129–153, 1961. 11 figs., 16 refs.

In a brief introductory review of the treatment of radiation injury by the use of bone marrow grafts the authors recall that one of the chief difficulties has been genetic incompatibility between the donor of the marrow and the recipient. They then report, from the Institute of Nuclear Studies, Oak Ridge, Tennessee, the results in 11 patients with acute leukaemia who were treated by total-body irradiation followed by attempted marrow transplantation. These patients, 7 children and 4 adults, were selected for treatment because of their poor immediate prognosis. Before irradiation, all treatment other than steroid therapy was stopped. Irradiation was carried out by means of a radioactive cobalt source and 10 of the 11 patients were treated by a single exposure.

The bone marrow for infusion was pooled from at least 4 homologous donors and was given intravenously on each of 5 days following irradiation, in a total dose equivalent to at least 6 billion cells. Two of the patients died within 48 hours of irradiation, 2 died later with marrow aplasia, and in 2 more there was temporary suppression of the leukaemia, but this was followed by exacerbation and death. Of 3 patients in whom partial suppression of the leukaemia was sustained for many weeks, 2 had been given no marrow after irradiation, and of 3 others whose leukaemia remitted with reappearance of apparently normal haematopoiesis, one had received no marrow infusion. All the remissions were of brief duration.

It is pointed out that since in cases of acute leukaemia total-body irradiation can result in remission even if marrow is not administered, it is therefore unjustified to regard a remission which follows irradiation and attempted homografting as evidence of success of the graft. Of the 3 patients who enjoyed remission, all 3 passed through a phase of marrow aplasia. It is therefore likely that in a proportion of cases of acute leukaemia total-body irradiation without marrow grafting might be followed by a remission if the patient could be tided over the aplastic phase by supportive therapy. It is possible that the cells of acute leukaemia are often so radiosensitive that irradiation may lead to massive cell death with unfortunate immediate consequences to the patient. The authors discuss their evidence that following a phase of irradiation-induced marrow aplasia regeneration of normal tissue occurs more rapidly in leukaemic patients than in normal subjects. They suggest that this may indicate an abnormality of the humoral control of the proliferation of normal bone marrow elements in acute leukacmia.

[This paper should be read in the original by all concerned with its subject; and particularly by anyone who is optimistic as to the possibilities of successful marrow homografting in the near future.]

A. G. Baikle

652. Alteration of Blood on Storage: Measurement of Adhesiveness of "Aging" Platelets and Leukocytes and their Removal by Filtration

R. L. SWANK. New England Journal of Medicine [New Engl. J. Med.] 265, 728-733, Oct. 12, 1961. 6 figs., 2 refs.

During routine storage of blood, the platelets and leukocytes, as well as adsorbed debris, form compact aggregates after 2 to 10 days' storage in acid-citrate-dextrose solution, and 16 to 24 hours' storage in heparin. This change can be detected by measurement of pressures necessary to force the blood through a microfilter with multiple pores 20 microns square. These aggregates can be efficiently removed by passage of the blood through glass wool or other wools made from synthetic or natural fibers.—[Author's summary.]

653. Haptoglobin: a Review. [In English]
E. R. Giblett. Vox sanguinis [Vox Sang. (Basel)] 6, 513-524, Sept. [received Dec.], 1961. Bibliography.

Respiratory System

654. Laryngeal Regulation of Respiration. [In English]
C. RATTENBORG. Acta anaesthesiologica Scandinavica
[Acta anaesth. scand.] 5, 129-140, 1961. 8 figs., 12 refs.

Working at Bispebjerg Hospital, Copenhagen, the author has studied the behaviour of the larynx during the expiratory phase of spontaneous respiration by direct observation, radiologically, and by time-constant studies. Direct observation was effected by placing one finger on the hyoid bone and another on the thyroid cartilage; approximation of these structures occurred during expiration and was found to be more pronounced during mouth breathing than during nose breathing; similarly, if graded resistances to expiration were added, the movements were reduced proportionately. Movements of the vocal cords were observed by direct and by indirect laryngoscopy.

In the radiographic studies, carried out on 7 normal subjects, lateral radiographs of the neck (for which the basic essentials of the technique employed are given) were taken during the middle phase of free exhalation while the subjects breathed successively through the mouth, the nose, and through interposed graded resistances of 3.5, 6.5, and 9.5 cm. H₂O per litre per second. An increase in the thyro-hyoid distance was taken to indicate an increased opening of the larynx; this was also accompanied by a widening of the laryngeal vestibule, measured by the distance between the epiglottis and the arytenoid region. A series of 4 radiographs is reproduced as an example of laryngeal expansion relative to the degree of resistance to exhalation.

The time-constant studies were performed by techniques described (the curves obtained are reproduced), a total of 34 normal subjects and 4 laryngectomized patients being investigated during exhalation through the mouth, both unimpeded and with interposed graded resistances. It was found, surprisingly, that the resistance time-constant curves of the laryngectomized patients corresponded to the lung model curve and to those of normal subjects.

Michael Kerr

655. Spontaneous Pneumothorax: a Review of 71 Cases R. G. STANEK, J. L. WILSON, and W. L. ROGERS. Diseases of the Chest [Dis. Chest] 40, 391-396, Oct., 1961. 11 refs.

The authors review 71 episodes of spontaneous pneumothorax which occurred in 67 male patients ranging in age from 19 to 77 years (but with 70% between 19 and 40) who were treated at the Veterans Administration Hospital; San Francisco, between 1947 and 1959. Of the 67 men 25 had been performing some active exertion such as lifting, walking, running, or coughing when the episode occurred, but the remainder were at rest, 9 being in bed; 19 (25%) gave histories of similar previous episodes. About two-thirds of them smoked 30 to 40 cigarettes a day, and only 3 were non-smokers. In 15

episodes there was an associated lung condition: of the remaining 56, pleural blebs were found at thoracoscopy or thoracotomy in 13 and they were assumed to be the cause in the other 43. Bed rest was the initial treatment in 19 cases and was successful in 17 of these, expansion of the lung occurring in an average of 17 days. The time for expansion was related to the original extent of the pneumothorax; the patients left hospital in an average period of 22 days. In the remaining 2 (in whom expansion failed to occur after 11 and 15 days respectively) and in a further 39 patients (55% of the series) treatment was by insertion of an intercostal catheter with suction at a negative pressure of 25 cm. H₂O for 3 days, followed by 2 days with a water seal to the catheter before removing it. The catheter was inserted at the time of thoracoscopy in most patients, but by means of a trocar in the rest. By this suction method of treatment the average time for expansion of the lung was 2 days and the average stay in hospital 12.5 days. There was no significant complication to this form of treatment, but the lung failed to expand in 4 cases and these were treated by thoracoscopy or thoracotomy.

The authors conclude that with a spontaneous pneumothorax of less than 20% bed rest alone is the treatment of choice. When the extent exceeds 20% then treatment by intercostal catheter suction is safe and effective. They suggest that thoracoscopy, in addition to radiology, is an important method of assessing whether catheter suction is likely to succeed or whether open thoracotomy will be required, and they have found that if performed at the time of inserting the catheter thoracoscopy is a simple and speedy procedure.

P. Hugh-Jones

LUNGS AND BRONCHI

656. Tobacco Smoking and Ventilatory Function of the Lungs

J. READ and T. SELBY. British Medical Journal [Brit. med. J.] 2, 1104-1108, Oct. 28, 1961. 4 figs., 11 refs.

This investigation to elucidate the effects of smoking on ventilatory capacity was carried out at Sydney Hóspital, Sydney, where bacterial pollution of the airways is less common than in Europe. The subjects numbered 302, consisting of ambulant out-patients with non-medical conditions, their friends, and members of the hospital staff. Detailed histories were taken and the maximum forced expiration was studied with a Wright peak flow-meter. "A non-smoker was regarded as a person who had never smoked more than one cigarette a day for one year. All ex-smokers had ceased smoking at least three months earlier, so that no difficulty arose in separating smokers from ex-smokers."

From the results there seems little doubt that in men smoking, even in the absence of symptoms, reduces ventilatory capacity. When cough and sputum are present there is even further reduction. If smoking ceases then there is a tendency to improvement in the results. In females the figures are comparable, but not so well defined. The findings could not be correlated exactly with the amount of smoking indulged in and the authors consider that both environmental and genetic factors may play a part in the final picture. There is ample and detailed statistical evidence to support their views on these aspects of the smoking problem.

Paul B. Woolley

657. Vanilic Diethylamide in the Management of Acute Respiratory Insufficiency: a Preliminary Report M. Aronovitch, L. M. Kahana, J. F. Meakins, R. E. G. Place, and R. Laing. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 875–885, Oct. 14, 1961. 6 figs., 7 refs.

This, is primarily a review from the Queen Mary Veterans' Hospital, Montreal, of modern methods of treating acute respiratory insufficiency in emphysematous subjects. Six case reports are presented and treatment. by tracheostomy with aspiration of secretions, mechani-'cal ventilation, bronchodilators, and antibiotics is described in detail. Clinical and biochemical improvement was observed in some patients with the use of vanillic diethylamide (a solution of 1 g. per 200 ml., infused intravenously at a rate of 30 drops per minute or given in doses of 100 mg. by intravenous injection at hourly intervals). The drug is thought to have a selective action on the respiratory centre and to have a greater margin of safety than other respiratory stimulants. It would seem to be a useful additional form of treatment in acute respiratory acidosis and may perhaps provide an alternative to tracheostomy in the milder forms of this disorder. T. Semple

658. Chronic Bronchitis in Great Britain

A NATIONAL SURVEY CARRIED OUT BY THE RESPIRATORY DISEASES STUDY GROUP OF THE COLLEGE OF GENERAL PRACTITIONERS. British Medical Journal [Brit. med. J.] 2, 973–979, Oct. 14, 1961. 19 refs.

A survey of respiratory symptoms was carried out in Great Britain among a random sample of the population between the ages of 40 and 64, in which 92 general practitioners took part. Of 1,630 individuals selected for study, 1,569 (787 men and 782 women) were seen, and the wives of 442 of the men were also interviewed. Respiratory symptoms were recorded on a standard questionary, and 5 consecutive estimations of ventilatory capacity were carried out with the Wright peak-flow meter. The diagnosis of chronic bronchitis was made by the doctors, using a standard method of inquiry.

Chronic bronchitis in the younger subjects was diagnosed almost as often in women as in men; but thereafter there was a steady increase with age for men, the prevalence being 17% in men and 8% in women and the total male:female ratio 2·13:1. The prevalence among men was 12% in rural districts compared with 23% in urban districts, and 6% for non-smokers compared with 18% for smokers. The difference as between social

classes ranged from 19% in Class IV to 6% in Class I. The results in women were less regular. Peak-flow meter readings as recorded by general practitioners were lower than those in 2 previous surveys carried out by specialist field workers, but were none the less of value as an additional means of assessing respiratory disability. The average readings were 32% lower in the bronchitics than in those without bronchitis.

G. M. Little

659. Chemotherapy of Bronchitis: Influence of Penicillin and Tetracycline Administered Daily, or Intermittently for Exacerbation

A REPORT TO THE RESEARCH COMMITTEE OF THE BRITISH TUBERCULOSIS ASSOCIATION BY ITS BRONCHITIS SUB-COMMITTEE. British Medical Journal [Brit. med. J.] 2, 979–985, Oct. 14, 1961. 4 refs.

A second controlled investigation of the use of antibiotics in the treatment of chronic bronchitis was carried out for the British Tuberculosis Association during the winter of 1959-60, the criteria being similar to those adopted for the first trial (Brit. med. J., 1960, 1, 297; Abstr. Wld Med., 1960, 28, 139). A number of the 551 patients from chest clinics throughout England, Wales, and Scotland who started the trial were excluded for various reasons, so that only 519 were included in the main analysis. Patients were allocated at random to one of 4 regimens: (1) tetracycline, 250 mg. twice daily throughout the trial; (2) penicillin-V (phenoxymethylpenicillin) potassium, 312 mg. twice daily throughout the trial; (3) tetracycline, 500 mg. thrice daily for 3 days at the onset of symptoms followed by 250 mg. thrice daily for 3 days; and (4) penicillin-V potassium, 624 mg. thrice daily for 3 days at the onset of symptoms followed by 312 mg. thrice daily for 3 days.

Patients receiving daily treatment with tetracycline (Group 1) showed a significant decrease in the number of working days lost from bronchitis when compared with the other 3 groups. Unlike the findings of the previous trial, the group given daily penicillin therapy did not do so well as that given daily tetracycline treatment.

Bacteriological studies were carried out in various laboratories, and the prevalence of *Haemophilus influenzae* in the sputum varied in different centres, probably owing to the different techniques used in culturing the sputum. The prevalence of pneumococci in the sputum was reduced by 75% when either antibiotic was given daily (Groups 1 and 2), but the carrier rate of *H. influenzae* was reduced only in patients receiving daily tetracycline treatment (Group 1).

G. M. Little

660. A Trial of Phenethicillin in Chronic Bronchitis R. N. JOHNSTON, W. LOCKHART, D. H. SMITH, and N. K. CADMAN. *British Medical Journal [Brit. med. J.]* 2, 985–986, Oct. 14, 1961. 5 refs.

This is the report of a double-blind controlled trial of phenethicillin carried out at the Chest Clinic, Dundee, on a group of 40 male patients with chronic bronchitis. Starting in October, 1960, treatment was continued for 6 months, the dosage of phenethicillin being 250 mg. twice daily. The authors noted the patient's subjective

assessment of his condition, the average work days lost per patient, the grade of dyspnoea, peak-flow reading, and resting and exercise ventilation. Using these criteria, they found no significant benefit from treatment with phenethicillin.

G. M. Little

661. Triancinolone in the Therapy of Chronic Bronchitis and Pulmonary Emphysema

L. J. CORAZZA, C. S. MORROW, and T. A. CHESNEY. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 436-442, Oct., 1961. 12 refs.

This paper from the Veterans Administration Hospital, Wilkes-Barre, Pennsylvania, reports the failure of triamcinolone to affect the ventilatory function or the levels of blood gases in 17 men with generalized airways obstruction due to chronic bronchitis and emphysema, 11 of whom had evidence of silicosis. The patients. most of whom were aged 60 to 69, were first given antibiotics and bronchodilators for 3 to 8 weeks, after which they all showed considerable clinical improvement. The initial pulmonary function tests were then carried out and triamcinolone given by mouth in doses of 4 mg. 8-hourly for 4 to 8 weeks, the administration of bronchodilators being continued during this time. Pulmonary function tests were then repeated, but showed little or no improvement. Most of the patients, however, reported some subjective improvement. C. M. Fletcher

662. Staphylococcal Pulmonary Infection

A. A. B. MITCHELL, R. I. S. DUNN, T. W. LEES, and C. K. HEDGES. *Lancet* [*Lancet*] 2, 669-672, Sept. 23, 1961. 12 refs.

From the experience of this hospital [Law Hospital. Carluke, Lanarkshire] we conclude that: (1) A major reservoir of hospital staphylococci, and a possible source of skin and wound infection, is the lungs of the patients. By reservoir we mean a discharging open pyogenic focus. (2) Patients who are in hospital for more than 7 days tend to become infected with hospital strains of Staphylococcus aureus in their lungs. (3) Patients admitted with chronic lung disease are more liable to develop lung sepsis associated with hospital staphylococci, than other patients. (4) Staphylococcal bronchopneumonia, or lung abscess, is a common accessory and occasionally a primary factor in death after abdominal operation, or indeed after admission to hospital at all. (5) The lung is a common primary site of staphylococcal septicaemia, and this may be a source of deep wound infection.

During the past 5 years bacteriological surveys of fomites, personnel, and equipment, as sources of staphylococcal infection, have been carried out in this hospital. Although appropriate counter-measures have been applied, such infection has persisted, as may be seen from the continued presence of *Staph. aureus* type 80.

It is questionable whether patients with chronic chest disease should be admitted to hospital unless this is essential. Admission often results in their deaths, even if the chest disability is not severe. What is more important, a possibly fatal infection may be transmitted to other patients. Some effort must be made to isolate patients with chronic and postoperative lung infections. Im-

perative surgery should be undertaken as soon as practicable after admission. Delay of a week greatly increases the hazards of staphylococcal infection, particularly of the lungs and particularly in patients with chronic bronchitis. Elective operations, particularly in patients over 65, should also be performed as soon as possible after admission, and only if the consequences of not operating are more likely to prove fatal. Protracted convalescence in hospital should be avoided.—[Authors' summary.]

663. The Value of Chloromycetin Succinate Used Topically in Intrathoracic Suppuration

J. G. STEVENSON, J. M. REID, N. McFARLANE, and J. D. BARRIE. British Journal of Diseases of the Chest [Brit. J. Dis. Chest] 55, 216–219, Oct., 1961. 3 refs.

The eradication of chronic intrathoracic suppuration is always difficult, even after effective surgical drainage combined with local deroofing rib resection. Since the infected pleura is relatively avascular, the authors considered the possibility of instilling antibiotic locally into the pleura, on the assumption that there would then be less risk of damage to the bone marrow. They used chloramphenicol succinate, which is the sodium salt of the monosuccinate ester of chloramphenicol; it is readily soluble in water. They now report their experience with this drug at the Royal Victoria Group of Hospitals, Glasgow, in 28 patients, all but 3 of whom had an intrathoracic empyema occurring either as a primary condition or secondary to surgical intervention. The investigation extended over 2 years.

After testing the sensitivity of the infecting organism 1 g. of the drug dissolved in 10 ml. of sterile water or saline solution was instilled daily for periods ranging between 8 and 90 days. In 19 cases the organism isolated was Staphylococcus aureus, resistant to penicillin in 17 cases; 2 patients had a coliform infection, one was infected with Pyocyaneus, one with a β -haemolytic streptococcus, and one with a mixture of coliform organisms and Pyocyaneus. In the remaining 4 cases, although numerous pus cells were seen, no organism could be grown on culture.

Serum levels of the drug were estimated and the amount excreted in the urine was also measured. Both these investigations showed a minimal absorption, the serum levels representing only 0 to 4% of those anticipated after a similar oral dose, and the excretion in the urine 0.6 to 2.3% of the figure expected if absorption from the topical application had approached that from the alimentary tract.

Three of the patients died; in 2 cases death was due to carcinoma, and the third patient died from uraemia as a result of chronic nephritis which had been present for many years.

The authors have formed the opinion that the topical use of chloramphenicol expedites healing in the empyema cavity, [but they do not state the exact course their cases followed]. Their results do, however, show that the drug can be given for long periods without toxic levels being reached in either the blood or urine.

Kenneth M. A. Perry

Urogenital System

664. The Relation between Glomerular Function and Histology in Acute Glomerulonephritis

A. E. PARRISH, N. C. KRAMER, F. E. HATCH, M. F. WATT, and J. S. HOWE. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 197–203, Aug., 1961. 2 figs., 12 refs.

At the District of Columbia General Hospital, Washington, D.C., 21 patients with acute glomerular nephritis were studied, some serially, by means of renal needle biopsy and subsequent determination of renal clearance of inulin and PAH. The renal pathology was graded on the basis of glomerular cellularity, basement membrane thickening, and degree of ischaemia and these features were correlated with the results of the renal clearance tests. The best correlation was between glomerular cellularity and glomerular filtration rate (inulin clearance). The ratio of glomerular to tubular function (G.F.R.: Tm PAH) tended to rise as the renal lesion improved histologically. Clinical recovery was usually associated either with good initial function or early rapid improvement of function. In some cases, however, histological abnormalities persisted for as long as 3 years, despite clinical and functional recovery. Deterioration of renal function was associated with progressive abnormal changes in the histological appear-K. G. Lowe

665. The Hemorrhagic Diathesis in Renal Disease (with Special Reference to Acute Uremia)

A. G. KENDALL, L. LOWENSTEIN, and R. O. MORGEN. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 405-411, Aug. 19, 1961. 4 figs., 43 refs.

The authors, who report from the Royal Victoria Hospital and University Clinic, McGill University, Montreal, have studied the haemorrhagic diathesis in 46 patients in acute or subacute renal failure. Capillary fragility was abnormal in only 6 out of 21 patients tested. In 27 there was a prolonged bleeding time. In all 46 cases the whole-blood glass clotting time was normal. A slight or moderate prolongation of the one-stage prothrombin time was seen in almost every case at or near the peak of azotaemia. In 10 out of 13 patients tested the plasma fibringen level was raised to 450 to 1,050 mg. per 100 ml. The thrombin clotting time was prolonged in 9 out of 14 patients tested. Among 27 patients the thromboplastin generation test of Biggs and Douglas often showed defective generation. Prothrombin consumption was abnormal in 27 out of 34 patients. A varying degree of thrombocytopenia was common; often accompanied by prolonged bleeding time and abnormal capillary fragility.

The authors conclude that their findings and those of other workers suggest that uraemic plasma has a deleterious effect on several sites in the sequence of blood coagulation, on the blood platelets and megakaryocytes, and directly or indirectly on the capillary wall. 666. Removal of Urea, Creatinine, Uric Acid, and Inorganic Phosphate by a Rotating-drum Artificial Kidney A. C. Kennedy, M. J. B. Gray, A. Dinwoodie, and A. L. Linton. Lancet [Lancet] 2, 996-999, Nov. 4, 1961. 2 figs., 13 refs.

This paper from the Royal Infirmary, Glasgow, reports the use of a rotating-drum artificial kidney with a large dialysing surface (3.2 sq. m.) in 10 patients with acute renal failure. Clearance rates were higher than with other forms of artificial kidney, not only for urea, but also for less diffusible substances such as creatinine, uric acid, and inorganic phosphate. The advantages of increased clearance in patients with trauma and consequent increased breakdown of tissue are emphasized.

D. A. K. Black

667. The Artificial Kidney and Urea Clearance D. J. BLACKMORE and W. J. ELDER. *Journal of Clinical Pathology* [J. clin. Path.] 14, 455-462, Sept., 1961. 8 figs., 9 refs.

The authors have studied the clearance of urea from the plasma of oliguric patients during haemodialysis on the twin-coil artificial kidney. The method adopted was to calculate the expected plasma urea level at the end of dialysis from the known initial plasma urea level and the rate of blood flow through the artificial kidney, assuming that urea is evenly distributed and freely diffusible throughout the body water and that the total body water constitutes 57% of the body weight. The calculated post-dialysis plasma urea level was then compared with the value actually found, and a figure derived which is described as an efficiency index for the dialysis-in each individual case.

Altogether 60 dialyses were assessed in this way. It was then found that the efficiency index appeared to bear some relation to the aetiology of the primary condition. Thus in 7 dialyses on 5 obstetric patients the actual and calculated efficiencies were very close, whereas 25 dialyses on 13 patients with trauma were less efficient in lowering the plasma urea level than predicted, and in 14 dialyses on 10 patients with glomerulonephritis the efficiency index was even lower. The remaining 14 dialyses in miscellaneous conditions produced a wide scatter of results.

The marked reduction in efficiency below the predicted value in the traumatic and glomerulonephritic cases could not be explained on the basis of increased urea production during the dialysis, because calculations showed that an increase in the rate of urea production to 3 times the normal would not significantly affect the efficiency index figure. The authors therefore postulate that urea may exist both in cell and plasma in non-diffusible as well as diffusible form; an increase in the ratio of non-diffusible to diffusible urea, particularly in patients with oliguria of traumatic or glomerulonephritic origin, would then account for the diminished efficiency of haemodialysis in lowering the plasma urea level in these cases.

M. Harington

Endocrinology

THYROID GLAND

668. Serologic and Immunohistochemical Study of Human and Experimental Thyroiditis

D. D. PORTER and R. H. FENNELL JR. New England Journal of Medicine [New Engl. J. Med.] 265, 830-834, Oct. 26, 1961. 4 figs., 31 refs.

At the Presbyterian, Woman's, and Eye and Ear Hospitals, Pittsburgh, 13 female patients with Hashimoto's thyrbiditis were studied in an attempt to correlate the serological and histological observations. In all cases the diagnosis was made histologically. Specimens of serum were studied by means of the complement fixation test, the tanned-erythrocyte agglutination test, the Hyland T.A. test, which employs latex particles coated with thyroglobulin, and the Ouchterlony precipitin reaction. For the precipitin test human thyroglobulin prepared by ammonium sulphate fractionation was used as the antigen. Extracts of thyrotoxic thyroid glands were used as antigens for the complement fixation test. In fluorescent antibody studies fluorescein isothiocyanate was conjugated with the patient's whole serum and the conjugated serum used as a stain on frozen sections of various specimens of human thyroid tissue, including thyrotoxic glands and glands of Hashimoto's thyroiditis.

Only 2 of the serum specimens examined showed precipitating antibody, one being associated with a low haemagglutination titre. The T.A. test gave negative results in these 2 cases, but gave positive results with 2 sera in which the presence of nuclear-localizing factor was shown by the fluorescence technique, but no thyroidspecific antibody was indicated by other tests. The complement fixation reaction was positive in 10 cases, being specific with the use of the thyrotoxic thyroid gland extract only in 9, and with extracts of normal brain, liver, kidney, and adrenal gland as well in one. No complement-fixing activity was found when purified thyroglobulin was used as antigen. The results of the fluorescent antibody study were closely similar, typical staining occurring only with sera showing specific thyrotoxic thyroid complement-fixing activity. The intensity of the fluorescent staining correlated with the complementfixing titre. The sera of high titre stained normal and thyrotoxic human tissue equally well, those of low titre staining normal thyroid tissue at most only weakly. Fluorescent staining of colloid occurred in 3 cases with sera showing no haemagglutinating titre, suggesting the presence in the colloid of microsomal proteins or small amounts of antithyroglobulin not detected by haemagglutination systems. Two sera gave intense staining of the nuclei of thyroid and other human tissue and the nuclei of dog, rabbit, and rat tissue, but not of colloid in any thyroid gland examined. No correlation between the presence or titre of antibody as measured by any

method and the degree of destruction of the thyroid gland was found in these patients.

Attempts were also made to produce thyroiditis in rabbits by the injection of thyroid extract from denor animals. Only in 3 out of 20 rabbits did his ological alteration of the thyroid gland occur in the form of focal accumulation of lymphocytes, eosinophils, and plasma cells around the thyroid follicles. The haemagglutination titres were raised, the precipitin reaction was positive, and the direct fluorescent antibody test showed very weak staining of colloid in these 3 rabbits. The complement fixation reaction was weakly positive in only one case.

Because of the great variability in the results of the serological tests and the lack of correlation between them and the degree of thyroid destruction found the authors suggest that the thyroid antibodies represent secondary manifestations of thyroiditis rather than pathogenetic agents. They consider that the finding of thyroid antibodies in subjects with no clinical thyroid disease supports this view.

Ferdinand Fok

669. A New Rapid Radioactive Iodine Test for the Assessment of Thyroid Function with Simultaneous Estimation of Peripheral Hormonal Iodine Supply. (Ein neuer Radiojodkurztest zur Schilddrüsenfunktionsprüfung mit gleichzeitiger Beurteilung der peripheren Hormonjodversorgung)

W. BÖRNER. Klinische Wochenschrift [Klin. Wschr.] 39, 990-998, Oct. 1, 1961. 4 figs., 40 refs.

The author reports his experience with a new rapid radioactive iodine test for the assessment of thyroid function which he has used in over 500 cases at the Medical Polyclinic of the University of Würzburg. In this test, which takes only 20 minutes to perform, the isotope 132I is used, since this has a short half-life and thus diminishes the amount of irradiation. Repetition of the test is possible and so is especially useful for checking the result of treatment. The main advantage of the rapid test in comparison with the normal or "long test", which requires 3 days to complete, seems to be the positive response which is obtained in cases of hypothyroid conditions. 132I (half-life 2.26 hours) is separated in the laboratory from radioactive tellurium (132Te), which is obtainable in the form of a solution of sodium tellurite from the Radiochemical Centre, Amersham. [The details of the technique must be read in the original paper.]

Two important points should be mentioned. In view of the rapidity of the test and for several other reasons (which are discussed) the tracer dose of 4 ml. of physiological sodium chloride solution of ¹³²I has to be injected intravenously within 2 seconds. Three curves are registered, one recorded from the neck, the second recorded from the thigh, while the third is the difference between the first and second curves and represents the actual uptake of iodine by the thyroid gland.

[There is a good discussion of possible sources of error in both the usual test and the rapid test and the paper merits reading in full by those concerned with carrying out such tests.]

V. C. Medvei

670. Hypothyroid Myopathy

K.-E. ASTROM, E. KUGELBERG, and R. MULLER. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 472–482, Nov., 1961. 5 figs., 17 refs.

This is a report of 8 cases of myxoedema admitted to Serafimerlasarettet, Stockholm, Sweden. The hypothyroid condition had been present for one to 8 years; 3 of the patients had received substitution therapy. All cases except one were examined clinically and electromyographically, and biopsy specimens of muscles were obtained. The remaining patient, a woman, died in a hypothyroid state shortly after her admission to hospital. and the pathological report is included. Five of the 7 patients fully investigated had definite paresis, most marked in the proximal muscles of the lower limb, although not always confined to them. The weakness appeared at the same time as the myxoedema in some cases, and several years later in others. In 2 of the 5 cases the muscular weakness persisted, though at the time of examination the patients were euthyroid as the result of substitution therapy. Only one patient complained of cramps. No hypertrophy or obvious atrophy of the muscles was seen in any case, nor were fasciculations observed.

Electromyographically, no gross reduction in the number of motor units was encountered. In every case, whether muscular weakness was present or not, pathological action potentials were found over small areas of the thigh muscles.

Definite pathological changes were found in all cases. Individual muscle fibres varied in size; some retained striations, others contained amorphous sarcoplasmic material and had pyknotic nuclei. In all cases there was acute degeneration in a few fibres. One case showed mucoid degeneration of segments of some muscle fibres in addition to the other changes.

It is suggested that the muscular weakness often complained of in myxocdema is not merely due to debility, but to a definite myopathy. E. H. Johnson

671. Incidence of Hypothyroidism and Recurrences following I¹³¹ Treatment of Hyperthyroidism. [In English] U. Beling and J. Einhorn. *Acta radiologica [Acta radiol. (Stockh.)*] **56**, 275–288, Oct., 1961. 3 figs., 41 refs.

At Radiumhemmet, Karolinska Sjukhuset, Stockholm, 791 patients who had received ¹³¹I treatment for hyperthyroidism were followed up for 2 to 8 years after the last treatment. By the end of one year 7.46% had developed hypothyroidism and about 3% of patients developed it in each succeeding year, so that after 7 years 26.5% showed evidence of thyroid deficiency. The sex distribution of this effect was even. The highest incidence was in patients whose hyperthyroidism had been without demonstrable thyroid enlargement (11.4% after one year, with an additional 15.3% by the end of

5 years). Many of these were patients in whom hyperthyroidism had recurred after surgical removal of the thyroid gland. Apart from this the incidence of hypothyroidism was not affected by the type or degree of gland' enlargement accompanying the initial overactivity. Hypothyroidism occurred more frequently among the younger patients in spite of a tendency to give them smaller doses of ¹³¹I. It was noted that patients who received ¹³¹I therapy-in a single dose seemed more likely to develop subsequent deficiency, while those whose treatment had been given in 4 or more doses showed a very low incidence of hypothyroidism.

Many patients develop a transient hypothyroidism immediately after ¹³¹I therapy which clears up without supplementary treatment and may be followed by a return of the hyperthyroidism if the dose of ¹³¹I has been insufficient. Apart from this rapid recurrence within a few months, hyperthyroidism rarely returns after treatment. On the other hand hypothyroidism following ¹³¹I treatment can develop late and be insidious in onset. The need for indefinite follow-up care after this treatment is therefore emphasized.

E. H. Johnson

672. Acute Myxoedema Precipitated by Pneumonia: Report of Five Cases

W. HAUSMANN and A. J. KARLISH. British Medical Journal [Brit. med. J.] 2, 1063-1065, Oct. 21, 1961. 6 refs.

Myxoedema is usually considered to be a chronic rather than an acute disease. The authors of this paper from the Combined Hospitals, Reading, describe 5 cases in which acute myxoedema, going on to coma in one case, developed during the course of pneumonia and indeed overshadowed the severity of the latter condition. All these cases occurred during cold weather, which may have been a contributory factor. It is suggested that there was already considerable damage to the thyroid tissue before the pneumonia developed, so that there was no reserve when the patient was subjected to extra stress.

B. M. Ansell

673. Natural History of Hashimoto's Disease (Involutional Thyroidosis). (Histoire naturelle de la maladie de Hashimoto (thyroidose involutive))

H. CHIMÈNES, H. P. KLOTZ, and C. SORS. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 37, 3175-3199, Nov. 20, 1961. 13 figs., bibliography.

The authors report from the Hôpital Bichat, Paris, an extensive study of 16 female patients with Hashimoto's disease together with a further 10 cases in which the diagnosis was less certain. In the first part of the paper they discuss the actiological background of this condition, which they believe may have an emotional or hormonal basis. The second part deals with the clinical features of this disease, and in particular the occurrence of hyperthyroidism and antithyroid antibodies in the blood of these patients.

The authors come to the conclusion that examination of a drill biopsy specimen, obtained by means of Drapier's apparatus, is the most accurate way of diagnosing Hashimoto's disease, and that autoimmune antibodies occur rather late in this disease. Finally the natural history of this condition is described. In some cases it started with hyperthyroidism, and in most cases ended with hypothyroidism requiring treatment with thyroid extract. The difficulties in treatment are fully discussed. A suggestion is made that cortisone in a dosage of 20 or 30 mg. a day will prevent further progress of the disease. The full clinical details of this interesting condition are presented in tabular form both for the 16 patients in whom the diagnosis was certain and the 10 other more doubtful cases.

I. McLean Baird

PARATHYROID GLANDS

674. Diagnosis of Primary Hyperparathyroidism: Clinical and Laboratory Aspects

F. R. Keating Jr. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 547-555, Nov. 11, 1961. 3 figs.

The author reviews the sum of knowledge relating to the diagnosis of primary hyperparathyroidism on the basis of 380 cases seen at the Mayo Clinic over 33 years.

Primary hyperparathyroidism was first described in 1926 as a rare bone disease. In 1934 it was reported by Albright *et al.* that the condition could occur in patients with little or no skeletal change, and that it could often be detected in patients with urinary calculi. Since this was pointed out it has been diagnosed much more frequently. Of the series here presented, 16 cases were found in the 15 years before 1943, when Albright's precepts were adopted, and 364 in the 18 subsequent years.

According to the system most prominently affected, three hyperparathyroid syndromes can be recognized: (1) a skeletal, (2) a urological, and (3) a hypercalcaemic syndrome. (1) Classic osteitis was present in 42 of the 380 patients. The extreme disorder described by Recklinghausen is a rarity, a mild degree of skeletal change associated with vague aches and pains being more common. (2) Symptoms of urinary calcinosis were experienced by 291 patients. The incidence of primary hyperparathyroidism in patients with urinary calculi has been reported as 5 to 10%. (3) Cases of hyperparathyroidism without either skeletal or renal involvement are now recognized with increasing frequency. Most of these cases are found by chance, but in some instances investigations are prompted by symptoms suggestive of hypercalcaemia; these include malaise, muscular weakness, bradycardia, polyuria, polydipsia, and gastrointestinal symptoms. Hypercalcaemic symptoms occurred in one-third of the author's cases, and in 26 these were severe.

Of diseases considered to be significantly associated with hyperparathyroidism, the author found peptic ulcer in 59 (15.5%) of his 380 cases. He suggests that in patients with peptic ulcer an investigation for hyperparathyroidism may be justified, especially if conventional treatment is followed by worsening of symptoms. Of another associated disease, pancreatitis, there were 10 instances (2.6%).

The diagnosis must rest very largely on the laboratory demonstration of hypercalcaemia for which other causes can be excluded. Of the original triad of cardinal biochemical changes—raised serum calcium level, lowered serum phosphate level, and excessive urinary excretion of calcium and phosphorus—hypercalcaemia has remained the ultimate criterion. The degree of hypercalcaemia may, however, at times be trivial. It is therefore important that investigations should be carried out in a laboratory where they are done frequently as a routine, and preferably in duplicate. The author emphasizes that clinical decisions should be based on mean values for calcium concentration derived from repeated estimations over a period of time, and never on isolated estimations.

The finding of hypophosphataemia is not essential for diagnosis. Of the author's 380 cases, only one had a normal serum calcium level—a finding based on one estimation alone. Normal values for serum phosphate concentration, however, were obtained in 41% of patients without azotaemia and in 89% of patients with a blood urea level of 40 mg. or more per 100 ml.

Excessive urinary excretion of calcium is the rule, but there are exceptions. The author found 18% of patients with hyperparathyroidism had normal renal function, and 55% of those with impaired renal function showed calciuria within the normal range. Alkaline phosphatase values are usually not increased unless there is clinically significant disease of bone.

Valuable in differentiating hyperparathyroidism from other causes of hypercalcaemia are: (1) reduced tubular reabsorption of phosphate; and (2) persistence of hypercalcaemia after administration of cortisone. But it is pointed out with regard to (1) that such reduction has also been found in renal insufficiency, osteomalacia, sarcoidosis, myeloma, and some renal tubular syndromes. Concerning (2) it is noted that large doses of cortisone given for a week or longer will completely suppress the hypercalcaemia of hypervitaminosis D, Boeck's sarcoid, thyrotoxicosis, multiple myeloma, and sometimes of carcinoma. The hypercalcaemia of primary hyperparathyroidism is not usually affected in this way, but the test is not infallible.

It is suggested that the only diagnostic criterion which might be comparable to estimation of the serum calcium level would be estimation of the serum concentration of parathyroid hormone, but no method for doing this yet exists.

Kenneth Stone

675. Carcinoma of the Parathyroid Glands: Report of 10 Cases with Endocrine Function

B. A. BARNES and O. COPE. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 556-559, Nov. 11, 1961. 25 refs.

Among over 250 cases of hyperfunctioning tumour of the parathyroid glands seen at Massachusetts General Hospital, Boston, 10 were found to be due to carcinoma. The authors, in reporting details of these cases, state that the condition is extremely rare, only about 50 examples having been recorded in the world literature. Of the 10 patients, 3 were male and 7 female, their ages ranging

from 26 to 61 years. A table is given showing the essential clinical and laboratory data. All cases gave unequivocal evidence of hyperparathyroidism, and were considered after repeated review by pathologists to have indisputable parathyroid carcinoma.

All 10 cases were treated surgically. At the time of writing 2 were alive and free from hyperparathyroidism and tumour recurrence, one 12 years and the other 3 years after excision of the tumour. One patient was still alive after 15 months, though showing evidence of hyperparathyroidism, possibly from an undetected metastasis. Of the 7 patients who died, 2 did so from causes unrelated to the parathyroid tumour. The remaining 5 died from hyperparathyroidism or from complications related to extension of the carcinoma. The interval from the time of diagnosis of parathyroid carcinoma to death varied from 4 days to 12 years.

The authors conclude that surgical treatment can lead to cure, but they point to the risk that it may cause dissemination of malignant cells. *Kenneth Stone*

GENITAL GLANDS

676: Urinary Oestrogen Measurements after Oophorectomy and Adrenalectomy for Advanced Breast Cancer W. T. IRVINE, E. H. AITKEN, D. F. RENDLEMAN, and P. J. FOLCA. Lancet [Lancet] 2, 791-796, Oct. 7, 1961. 4 figs., 28 refs.

It is now clear that oophorectomy and adrenalectomy or hypophysectomy will cause a temporary regression of advanced breast cancer in some cases but not in all. Many attempts to find a means of predicting the probable response to endocrine surgery have been made, and recent work on these lines is reviewed in this paper from the London and St. Mary's Hospitals, London. Measurement of the urinary excretion of androgens and oestrogens before and after operation has hitherto produced inconclusive results and the present authors have now tried a more sensitive method of measuring urinary oestrogens in the hope of detecting finer differences which might aid prognosis. The investigation was carried out on 54 patients aged from 39 to 68 (mean 50.4) years, of whom 12 were premenopausal and 12 of the remaining 42 were not more than 5 years postmenopausal: Bilateral adrenalectomy and oophrectomy were performed in most cases, but 5 of the premenopausal patients underwent oophrectomy only.

The method of assessment of the response to surgery was strictly objective. Accurate measurements of the breast tumour and skin metastases were made and radiographs of the chest and bony metastases taken before operation. Any liver enlargement and neurological signs were carefully noted so that regression after operation could be assessed. The urinary oestrogen content was determined on samples of pooled 3-day collections of urine both before and after operation. The urine was hydrolysed, subjected to chromatography on a "celite" column, and estimated fluorimetrically according to the method of Preedy and Aitken (J. biol. Chem., 1961, 236, 1297). In view of the low oestrogen levels in

these patients double chromatography of the extracts was carried out. Amounts of oestrone, oestradiol, and oestriol above 0.1 µg. per 24 hours were measured; all methods are fully described. Objective evidence of the response to endocrine surgery was compared with the level of oestrogen excretion. No significant difference in the excretion level between responders and nonresponders was found, a result in accordance with that of previous workers. In their summing up the authors comment that an over-all remission rate of 40% following endocrine surgery is probably an optimistic assessment and that in many cases such remission is not of sufficient duration to justify major surgery unless more reliable means of predicting the probable outcome of operation can be found. Nancy Gough

677. Studies with Tritium-labelled Hexoestrol in Advanced Breast Cancer

P. J. FOLCA, R. F. GLASCOCK, and W. T. IRVINE. *Lancet* [Lancet] 2, 796-798, Oct. 7, 1961. 1 fig., 8 refs.

The finding that urinary oestrogen excretion is not reliably correlated with the response to adrenalectomy and oophorectomy in patients with advanced breast cancer does not exclude the possibility that such response may be nevertheless in some way related to oestrogen metabolism. In this further study therefore [see Abstract 676] the authors have investigated the capacity of tumour tissue to accumulate oestrogen, and the relation of this capacity to clinical response to endocrine surgery. Following up the work by Burgos-Gonzalez and Glascock (Biochem. J., 1960, 74, 33) the tissue accumulation of tritium-labelled hexoestrol was determined in 10 patients undergoing bilateral adrenalectomy and oophorectomy or radical mastectomy, these 10 being selected because they all had palpable skin metastases which made for convenience of biopsy. Hexoestrol labelled with radioactive tritium was prepared by the method of Glascock and Pope (Biochem. J., 1960, 75, 328) and 100 µg. injected intravenously 6 hours before operation. Samples of blood, striated muscle, and metastatic tumour tissue removed at operation were then assayed for tritium by the gas-counting method of Glascock (Isotopic Gas Analysis for Blochemists, New York, 1954). The nitrogen content of the tissue was also determined so that the hexoestrol content could be expressed in mug. per g. of nitrogen.

The range of concentration of hexoestrol in tumour tissue was found to be higher than that in either muscle or blood, these last tissues showing roughly similar levels. Moreover, the patients with the highest concentration of hexoestrol in tumour tissue were those who showed most improvement after operation. In these patients the ratio of hexoestrol in tumour tissue to that in muscle ranged from 3-0 to 9-3 compared with ratios of from 0-86 to 2-4 in those who did not improve. No definite conclusion can be based on this small number of patients, but the authors suggest that further work should indicate whether it is possible to relate high capacity of tumour tissue to accumulate hexoestrol with probable benefit from endocrine surgery. If confirmed, this would be of great value in the selection of patients, at

least those with superficial metastases, for this type of operation. The technique is at present time-consuming and exacting, but various proposed improvements now under consideration are mentioned.

Nancy Gough

PANCREAS

678. Hyperinsulinism in the Pathogenesis of Neuroglycopenic Syndromes

V. MARKS, D. MARRACK, and F. C. Rose. Proceedings of the Royal Society of Medicine [Proc. roy. Soc. Med.] 54, 747-749, Sept., 1961. 1 fig., 17 refs.

The authors point out that hyperinsulinism due to tumour of the pancreatic islet cells may cause symptoms closely resembling any one of a number of organic or functional nervous disorders. The failure to take this possibility into consideration is the most usual cause for misdiagnosis in such cases. Of 16 cases, of which 9 were seen within the past 2½ years, the authors were able to make histological studies in 13. The tumour was benign in 7, recurrent and multiple in one, metastatic in 4, and probably malignant in one other; 3 of the patients refused operation. The authors describe as neuroglycopenic those symptoms and signs which develop when the supply of metabolizable carbohydrate available to the neurone is inadequate. They stress that hypoglycaemia may occur without neuroglycopenia, and vice versa. They classify the neuroglycopenic syndromes which occur in patients with hyperinsulinism into the following four types: acute, subacute, chronic, and hyperinsulin neuronopathy.

In the acute type, which is most commonly caused by insulin overdosage, sweating, vasodilatation, hunger, numbness of the tongue and lips, tachycardia, diplopia, and unsteady gait are the characteristic symptoms, and these may be followed by coma in severe cases. In the authors' opinion the part which adrenaline plays in producing these symptoms has been exaggerated. Subacute neurological symptoms, which are common in cases of insulinoma, may in some patients be associated with a progressive loss of intellectual ability accompanied by lassitude which gradually merges into stupor and coma, while other cases may present a more chronic clinical picture manifested by a variety of psychiatric syndromes which may be variously diagnosed as hysteria, schizophrenia, or organic dementia. Hyperinsulinism neuronopathy probably represents a specific example of irreversible neronal damage resulting from profound neuroglycopenia.

However, the pathogenesis of neural dysfunction in hyperinsulinism is not clear. The blood glucose level does not necessarily reflect the utilization of glucose by the brain, and it is possible that the rate of change in level rather than the absolute level of glucose in the blood is responsible for producing symptoms. It has also been suggested that there is an adaptive mechanism which permits adjustment of neural metabolism to abnormally low blood sugar levels. It may be that the low blood sugar level is not the sole cause of cerebral dysfunction and the hypothesis has been advanced that

insulin may be toxic, especially in the presence of low tissue glucose concentration, but the mechanism is not fully understood.

John Lister

679. Glucagon and Tolbutamide Tests in the Recognition of Insulinomas

D. MARRACK, F. C. Rose, and V. MARKS. Proceedings of the Royal Society of Medicine [Proc. roy. Soc. Med.] 54, 749-752, Sept., 1961. 5 figs., 10 refs.

The authors point out the need for a simple and reliable procedure for the diagnosis of hyperinsulinism due to insulinoma [see Abstract 678]. Previous studies of the effects of glucagon and tolbutamide on the blood glucose concentration and the development of neuroglycopenia in cases of insulinoma have suggested that these drugs appear to meet the requirement. Thus it has been shown that intramuscular administration of glucagon can precipitate neuroglycopenia in the presence of an abnormally low blood glucose level.

In the present study 33 control subjects and 10 patients with insulinoma were each given 1 mg, of glucagon by intramuscular injection. Two features were observed: (1) a rise in the blood glucose level of not less than 40 mg. per 100 ml. between 15 and 30 minutes after the injection of glucagon, followed by (2) a fall in the blood glucose level to less than 45 mg, per 100 ml, at or before 180 minutes, with little if any subsequent rise. Of 10 patients with insulinoma the fasting blood sugar level was low in 6 before starting the test, but only one had symptoms at this time and these disappeared as the blood sugar level rose during the test and reappeared as it fell; in one case the test had to be stopped on account of neuroglycopenia. The mean rise in blood glucose levels in the 10 patients with insulinoma was similar to that in the control group, but in contrast to the controls all developed hypoglycaemia within 1½ to 3 hours after injection of glucagon. Two patients with reactive hyperinsulinism showed a. normal response.

In the tolbutamide test 1 g. of sodium tolbutamide in 15 to 20 ml. of distilled water is given intravenously and the extent of the fall and subsequent restitution of glucose concentration in capillary blood is followed for the next 3 hours. In patients with insulinoma the abnormal feature is the failure of the blood glucose level to rise again after the initial fall, whereas in normal subjects it always returns to at least 70% and usually 80% of the fasting level after 3 hours. Of 6 patients with insulinoma studied, the characteristic fall in blood glucose concentration was seen in 3, while in the remaining 3 there was little change in this concentration but severe neuroglycopenia developed in 2 and mild neuroglycopenia in 1. False positive results in the tolbutamide test have been reported in patients with liver disease, pituitary tumour, and the pluriglandular syndrome.

The authors point out that one of the diagnostic difficulties with insulinoma is that the tumour grows slowly and the symptoms are progressive. The advanced case with severe neural damage is easily recognized by the fact that a period of fasting causes hypoglycaemia, but the detection of early cases before there is neuronal disorganization is more difficult. The two tests described, however, do seem to offer a partial solution and have the advantage that in doubtful cases they can be repeated after an interval.

John Lister

680. Experimental Research on Diabetes Mellitus. [Litchfield Lecture]

F. G. YOUNG. British Medical Journal [Brit. med. J.] 2, 1449–1454, Dec. 2, 1961. 3 figs., bibliography.

681. Diabetes Mellitus Complicated by Bacteremia Caused by Gram-negative Bacilli: Further Observations W. J. MARTIN and M. C. McHenry. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 36, 507-516, Sept. 27 [received Nov.], 1961. 33 refs.

In a previous report from the Mayo Clinic (A.M.A. Arch. intern. Med., 1957, 100, 214) it had been noted that diabetes was present in 10% of a group of 137 cases of bacteriaemia due to Gram-negative bacilli. In other reports a similar high incidence of diabetes has been recorded, and the present paper reviews a further 113 cases of bacteriaemia in 12 of which diabetes was present.

The organism concerned was Escherichia coll in 6 cases, Aerobacter aerogenes in 5 cases, and Salmonella enteritidis in one case. The usual portal of entry was the genitourinary tract consequent upon some operative procedure such as prostatic resection, cystoscopy, or the insertion of an indwelling catheter. All the cases except one were in men, presumably owing to the high incidence of genitourinary surgery in males. All the 12 patients were acutely ill, and a number of them went into a state of severe shock, which led in one case to a diagnosis of hypoglycaemic reaction. All the cases were treated with tetracycline, and in a number of instances other antibiotics were given as well. Two patients died.

The authors stress the importance of considering bacteriaemia in diabetic patients, especially those who have undergone surgery on the genito-urinary tract, and also in those patients who develop signs of shock. They emphasize that treatment should be based on the assumption that bacteriaemia may be present before the results of blood culture are available.

T. D. Kellock

682. Occurrence of Diabetes Mellitus in Families of Patients with Cystic Fibrosis of the Pancreas

R. N. CHARLES and M. L. KELLEY JR. Journal of Chronic Diseases [J. chron. Dis.] 14, 381-385, Oct., 1961. 15 refs.

There is increasing evidence that mucoviscidosis is not only a fatal disease of early childhood but has relevance to other problems in general medicine. The genetic aetiology and the occurrence of incomplete and minor forms of the disease raise the possibility of an association with diabetes mellitus. The authors of this paper from the University of Rochester School of Medicine and Dentistry, New York, studied the family histories of 25 unrelated patients with cystic fibrosis of the pancreas seen over a period of 5 years. Of the 25 patients 11 had a close relative with diabetes mellitus and the mothers of 3 of these 11 patients had been diabetic at the time of delivery. The incidence of familial diabetes in a somewhat comparable series of patients with

coeliac disease was 1%. A further comparison was made with three groups, each of 40 patients under the age of 25, who were admitted respectively for diarrhoea of undetermined cause, acute bronchitis, and tonsillectomy. A family history of diabetes was present in 12.5%, 12.5%, and 5% of these groups respectively. A familial association of mucoviscidosis with diabetes has not previously been recorded. However, an association with chronic pulmonary disease and with peptic ulcer has been noted. The occurrence of diabetes in patients with cystic fibrosis of the pancreas appears, from the literature, to be very infrequent and the significance of the present findings is problematical.

H.-J. B. Galbraith

683. Effect of Unrestricted Diet on Diabetes during Therapy with Chlorpropamide

K. M. West and E. Tophøj. Metabolism: Clinical and Experimental [Metabolism] 10, 689-694, Sept., 1961.

The effects of unrestricted diet were observed over periods of 3 to 26 months in 23 maturity-onset diabetics during therapy with 125–250 mg. chlorpropamide a day. In spite of the lack of dietary restrictions, chlorpropamide usually produced a hypoglycaemic effect. However, 18 of the 23 subjects gained weight, and when weight gain was great, the control of diabetes was unsatisfactory in spite of chlorpropamide. Patients whose fasting blood glucose levels exceeded 200 mg. per 100 ml. before therapy were not controlled satisfactorily on this regimen. However, in 10 of the 23 patients, control was "good" (fasting blood glucose below 110 mg. per 100 ml.) in spite of unrestricted diet. These 10 all had very mild diabetes and probably would have responded to diet alone.

.Under the conditions of our observations, the glucose tolerance of individuals treated with unrestricted diet and chlorpropamide remained unchanged, with rare exceptions.—[Authors' summary.]

684. Elevated Levels of Serum Insulin-like Activity (ILA) as Measured with Adipose Tissue in Early Untreated Diabetes and Prediabetes

J. STEINKE, R. CAMERINI, A. MARBLE, and A. E. RENOLD. *Metabolism: Clinical and Experimental [Metabolism]* 10, 707–711, Sept., 1961. 1 fig., 15 refs.

It was first demonstrated by Bornstein and Lawrence (Brit. med. J., 1951, 1, 732) that when insulin-like activity (I.L.A.) in the plasma was estimated by the rat hemidiaphragm technique normal levels of I.L.A. were obtained in untreated diabetic patients with onset of the disease in adult life, but not in those with the more severe form of diabetes with onset in youth. However, Steinke et al. (Lancet, 1961, 1, 30) showed that when I.L.A. was estimated by the rat epididymal-fat technique it was found to be raised in the serum of patients with untreated diabetes of both types. This discrepancy, it was suggested, may result from the presence of an insulin antagonist which is effective on the diaphragm preparation but not on adipose tissue.

In this preliminary report from Harvard Medical School the authors now describe further observations on serum I.L.A. as estimated with adipose tissue in a group

of subjects classified as prediabetic on genetic grounds, for example, those with 2 diabetic parents or a diabetic identical twin; I.L.A. was also determined in 33 control subjects and 31 patients with early, untreated diabetes. The bioassay method used was that based on the oxidation by adipose tissue of glucose labelled with radioactive carbon. Significantly raised levels of I.L.A. were found in both the prediabetic and untreated diabetic groups, and in the latter group the level was raised in the patients with the youth-onset form of diabetes as well as in those with the adult-onset form. The authors conclude that although these findings do not establish that the activity measured represents insulin only, the anomaly which appears to precede the onset of diabetes calls for further study. · K. O. Black

685. Factors Influencing Oral Glucose Tolerance: Experience with Chronically Ill Patients

A. HECHT, S. WEISENFELD, and M. G. GOLDNER. *Metabolism: Clinical and Experimental [Metabolism]* 10, 712–723, Sept., 1961. 2 figs., 20 refs.

A total of 42 chronically ill, hospitalized patients and 15 normal adults underwent 107 oral glucose tolerance tests. Glucose was determined by the Somogyi-Nelson microtechnique using capillary fingertip blood in all tests. In 29 subjects, both capillary and venous bloods were used. In 11 subjects, tests were repeated in from 6 to 342 days, with 6 of the subjects receiving a high carbohydrate diet for 3 days and 1 a low carbohydrate diet for 2 weeks prior to one of the repeated tests. Oral glucose tolerance tests were sufficiently reproducible to suggest the same interpretation on repeated tests. Carbohydrate prefeeding did not improve dextrose tolerance, nor did a low carbohydrate diet alter it. Oral glucose tolerance decreased with age and with chronic hospitalizing illness. The amount of physical activity within the institution did not affect the glucose tolerance curves. Capillary blood sugar was higher in most cases than venous blood sugar; this difference was more marked after dextrose ingestion. In general, capillary blood sugar did not return to fasting level until 3 hours after glucose ingestion. A revision of the usual criteria for the oral glucose tolerance test is needed when capillary blood is used. Speci--fic criteria must also be established for both capillary and venous oral glucose tolerance tests in older age groups and hospitalized patients.—[Authors' summary.]

686. Concerning the Mechanisms of Insulin Action. [Banting Memorial Lecture 1961]
R. Levine. *Diabetes* [Diabetes] 10, 421-431, Nov.-Dec., 1961. 16 figs., bibliography.

687. Chlorpropamide in Patients on High Insulin Dosage D. L. Singer, R. C. Stewart, and D. Hurwitz. New England Journal of Medicine [New Engl. J. Med.] 265, 823–826, Oct. 26, 1961. 1 fig., 10 refs.

At Boston City Hospital 28 out-patients with diabetes of the maturity-onset type requiring large doses of insulin were transferred to treatment with chlorpropamide. None of the patients had a history of diabetic acidosis (defined as a blood carbon dioxide content below 15

mEq. per litre). They included 10 males and 18 females between 45 and 79 years of age with duration of diabetes ranging from one to 31 years, the age at onset being 32 to 71 years. The patients had been requiring between 50 and 230 units of insulin per day for at least 60 days. before the transfer to chlorpropamide. Insulin was abruptly withdrawn and the administration of 0.5 g. of chlorpropamide daily started. They were seen in the clinic on the first and second days and then at weekly intervals until definite control had been established. Polyuria, polydipsia, or ketonuria was regarded as a sign of primary failure, but not glycosuria alone, which frequently took 4 to 6 weeks to cease. Failure of the blood sugar level to fall below 200 mg. per 100 ml. within 8 weeks also indicated primary failure. The postprandial blood sugar level was determined, a fasting sample of urine tested for sugar, acetone, and protein, and the patient's weight recorded at each visit. No alterations in the diabetic diet were made. The dosage of chlorpropamide was adjusted during the trial and 0.5 g. was eventually adopted as the maximum daily dose as patients not controlled by this dose could seldom be improved by increasing it. The abrupt transfer from a high dosage of insulin to chlorpropamide was proved to be safe, as none of the patients manifested acidosis or other severe diabetic symptoms. There was no evidence. of toxic effects of chlorpropamide, and hypoglycaemia was not a problem.

Of the 28 patients, 14 (50%) responded to the drug. Of these, 3 failed to maintain control after periods of 7, 8, and 20 months respectively and were classified as secondary failures. Of the remainder, the results in 5 (17.9%) were considered excellent, in 3 (10.7%) good, and in 3 (10.7%) fair, the postprandial blood sugar level on 75% of occasions being below 110, 150, and 200 mg. per 100 ml. respectively in these 3 categories. No significant differences in age at onset of diabetes, duration of diabetes and insulin treatment, age and dosage of insulin at the time of study, maximum dose of insulin, or weight were found between the responding and non-responding groups.

In all the 14 patients who responded initially to chlorpropamide, substitution of a placebo for the drug resulted in a recurrence of glycosuria, hyperglycaemia, and diabetic symptoms. Six patients had previously been given tolbutamide; the 2 who had responded to tolbutamide also responded, with better control, to chlorpropamide, whereas the remaining 4 responded to neither drug. Only 5 of the 28 patients were satisfactorily controlled with insulin before the transfer; all these responded to chlorpropamide, but one became a secondary failure. All patients classified as primary failure on chlorpropamide were poorly controlled with insulin also.

It is suggested that the patients who respond successfully to chlorpropamide are those with mild diabetes who for certain reasons, such as increased degradation, binding, or inactivation of exogenous insulin, do not respond to ordinary amounts of administered insulin. Trial and error is considered to be the only method at present available for selecting the patients who will respond to chlorpropamide.

Ferdinand Fok

The Rheumatic Diseases

688. Experimental Reactivation of Subsiding Rheumatic Rever

A. R. Feinstein and M. Spagnuolo. Journal of Clinical Investigation [J. clin. Invest.] 40, 1891–1899, Oct., 1961. 2 figs., 11 refs.

The authors report from Irvington House, Irvingtonon-Hudson, and New York University School of Medicine a further clinical and laboratory study of the relapses which occur following cessation of salicylate or steroid therapy in patients with rheumatic fever. In their previous studies of this rebound phenomenon (Yale J. Biol. Med., 1961, 33, 259 and 279; Abstr. Wld Med., 1961, 30, 230) evidence was obtained which suggested that such relapses represent the reappearance of the inflammation that had been suppressed during therapy. In the present study 88 patients aged 4 to 18 years who had not received anti-inflammatory therapy for one month and who then showed no clinical evidence of active rheumatic disease were given experimental re-treatment for a period of 2 weeks. Consecutive patients were allocated to one of 3 treatment groups which received respectively: prednisone in a dosage of 60 mg, per day for one week and 40 mg, per day for the second week (29 patients); aspirin, 0.75 grain per lb. (110 mg. per kg.) body weight per day for one week and 0.5 grain per lb. (70 mg. per kg.) per day for the second week (29 patients); the remaining 30 patients received no therapy and served as controls.

On cessation of therapy, clinical relapse was observed in 9 of the patients who had received prednisone, in one who had received aspirin, and in none in the control group. Laboratory relapse (shown by a rise either in the erythrocyte sedimentation rate or in the C-reactive protein level) occurred in 13, 3, and 3 patients in the three groups respectively. In the prednisone-treated group the incidence of relapse depended to some extent on the nature of the cardiac condition. Thus relapses occurred in 3 of 11 patients with no valvular involvement, in 2 out of 11 with valvular involvement and no significant cardiomegaly, and in 4 of 7 with significant cardiomegaly. In the aspirin-treated group relapse occurred only in one patient of the 7 with significant cardiomegaly. No relapse was observed in the untreated group whatever the cardiac state. Analysis of the case records revealed that clinical relapses after the experimental course, of therapy occurred only in those patients who had previously shown clinical or laboratory evidence of disease activity following an earlier course of treatment which had included steroids.

The authors conclude that these findings support their hypothesis that post-treatment relapses are due to a resumption of the inflammatory process previously suppressed and show that anti-inflammatory drugs, particularly steroids, should be avoided in patients with rheumatic fever but without acute clinical manifestations.

Hewett A. Ellis

689. The Prophylaxis of Recurrence of Rheumatic Fever. (Rezidivprophylaxe des rheumatischen Fiebers) A. Dortmann, F. Küster, and K. Völkel. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 86, 1995–1998, Oct. 20, 1961. 12 refs.

The authors, working at the Children's Hospital. Essen, have noted that rheumatic fever in German children now runs a much milder course than formerly, and that deaths during the first attack are now very rare. On the other hand there is little evidence that rheumatic fever is becoming any less common and the tendency to relapses is as high as ever. It is estimated that a relapse will occur in one out of every 3 children within 5 years of the first attack. Prevention of these relapses is therefore of great importance and the authors report the effect of oral penicillin prophylaxis on the relapse rate in three groups of patients: (1) 55 who regularly and daily took 200,000 units of phenoxymethylpenicillin by mouth; in an average period of 2 years follow-up only one patient suffered a relapse. (2) Among 29 other patients who were prescribed the same treatment but were irregular in taking the drug 2 suffered a relapse. (3) Finally. of 70 patients who were not given any prophylactic treatment 19 relapsed. These findings emphasize the necessity of continuous prophylaxis, which must be enforced even though it is tedious to children. John Lorber

690. Serological Reactions in Inflammatory and Noninflammatory Diseases of the Spine and Joints. (Serologische Reaktionen bei entztindlichen und nichtentzündlichen Affektionen der Wirbelsäule und der Gelenke)

N. FELLMANN and M. ENDERLIN. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 86, 1956–1960, Oct. 13, 1961. 2 figs., 22 refs.

In this paper from the University of Zürich the authors report the results of the following serological investigations carried out on 930 patients with arthritic complaints: determination of the antistreptolysin titre, streptococcal agglutination, and antiglobulin consumption test, appearance of the L.E. phenomenon, various agglutination reactions with latex and Fraction II, and the Bentonite flocculation test.

By analysing the percentage of positive reactions obtained in various inflammatory and non-inflammatory diseases the following four types could be distinguished:
(1) The streptococcal type; this was confined to cases of rheumatic fever, which all showed a high antistreptolysin titre, but negative results with the other tests.
(2) The agglutinating type; this group included cases of rheumatoid arthritis and periarteritis nodosa and in these there was a high percentage of positive results with various agglutination tests. (3) The L.E. type was seen in cases of lupus erythematosus, which nearly always gave positive results with the antinuclear factors and a high

percentage of positive results with the agglutination reactions. (4) The non-reactors. These included patients with osteoarthritis or gout and the control group of patients with non-arthritic conditions. It was noted that scleroderma seemed to fall between Types 2 and 3, giving a high percentage of positive reactions in the antiglobulin consumption test.

H. F. Reichenfeld

691. The Effect of Hyperventilation on Rheumatold Arthritis

F. H. KAHN, D. H. SIMMONS, and H. J. WEINBERGER. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 342–355, Aug., 1961. 7 figs., 27 refs.

The investigation herein reported was designed to test the hypothesis that the efficacy of aspirin in the rheumatic diseases is related causally to the results of the hyperventilation it produces, since similar symptomatic improvement in rheumatoid arthritis has been observed with other hyperventilatory conditions such as fever, hot baths, and pregnancy. The effects of aspirin were compared with those of hyperventilation produced by the Drinker respirator in 4 healthy subjects and 19 patients with arthritis [specified]. The values assessed were the subjective status of the patient (by replies to questions) and the range of joint motion during aspirin administration, after aspirin had been withdrawn for 48 hours, after 3 to 6 hours in the respirator, and finally after cessation of passive respiration. The alveolar-carbon dioxide tension (pCO2) was measured by an infrared gas analyzer, and the serum salicylate concentration, the erythrocyte sedimentation rate (E.S.R.), the C-reactive protein value, cosinophil count, and plasma 17-hydroxycorticosteroid levels were determined.

Symptomatic improvement occurred within one hour from the start of hyperventilation in 15 experiments and was associated with a marked decrease in alveolar pCO2 in all except one patient who had gout. Active hyperventilation persisted after removal from the iron lung in 14 out of 19 experiments for a mean period of 7 hours (0.5 to 29 hours) and was accompanied by continued freedom from symptoms. There was correlation between improvement in the range of motion and the alveolar pCO₂; the clinical state appeared to correlate better with alveolar pCO2 than with the serum salicylate level. The E.S.R. fell significantly in 9 out of 13 markedly hyperventilated patients. The values for serum C-reactive protein and pain threshold were not significantly altered. Patients with Reiter's syndrome, gout, and ankylosing spondylitis also improved. The mechanisms of this effect remain obscure. E. G. L. Bywaters

692. Involvement of the Hips in Juvenile Rheumatoid Arthritis

F. JAQUELINE, A. BOUJOT, and L. CANET. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 500-513, Oct., 1961. 5 figs., 29 refs.

The clinical and radiological features of involvement of the hip-joint in juvenile rheumatoid arthritis were studied in 85 patients at the Hôpital Reine Hortense, Aix-les-Bains. Of 54 of the patients in whom coxitis developed before the age of 15, 27 had been examined

in childhood and the course of the disease was actually observed for 1 to 5 years in 11 and for 6 to 16 years in a further 11. Of the 27 with coxitis who first came under observation after the age of 15 some were examined much later, even as long as 45 years after the onset of the disease. The hip-joint was usually affected at an early stage—in 29 cases during the first year of the disease. Radiologically, osteoporosis was the first change observed; it was already visible in one case of only 3 months' duration. The authors state that osteoporosis begins in the cephalic epiphysis and spreads to the femoral shaft and the bones of the pelvis. The outline of the joint, often irregular in childhood, is still more distorted by the disease. Narrowing of the articular space is a late manifestation and may be slight, as in one severè case of 6 years' duration (of which radiographs are reproduced). Premature fusion of the constituent bones of the acetabulum or upper end of the femur may occur. The fusion may be faulty with persistent cartilage at the lines of union. Accelerated fusion can lead to premature arrest of bone development in the femoral head and in the pelvic bones; such arrest-in development is often irregular, producing pelvic assymetry or marked disharmony between the constituents of the hip-joint. -In 24 joints there was a marked valgus deformity of the femoral head and in 5 the deformity was varus. There was some degree of subluxation in 20 hip-joints. It is pointed out that bone destruction leads to collapse of the femoral head and accelerates the subluxation. Large osteophytes frequently develop on the upper rim of the acetabulum. In 3 cases osteoporosis was the only sign of involvement. Bony ankylosis was observed in 5 cases, but 4 of these with destructive lesions in the vertebrae were regarded as cases of ankylosing spondylitis. William Hughes

693. Zoxazolamine as a Uricosuric Agent. I. Acute Effects in Healthy Non-gouty Subjects

E. B. REED, T. V. FEICHTMEIR, and S. G. CRAIG. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 533-551, Oct., 1961. 9 figs., 46 refs.

The authors have studied the uricosuric action of zoxazolamine, a compound which is not related to a wide variety of agents (including probenicid, phenylbutazone, and bishydroxycoumarin) that have previously been found to increase urate clearance in human beings. This pharmacological action is believed to be due to interference with tubular reabsorption of urate in the kidney, but there is no single component shared by these drugs to which one such constant uricosuric effect can be attributed. It has been established that the response to uricosuric agents of non-gouty subjects is essentially the same as that of patients with gout. The effects of zoxazolamine were assessed in 35 healthy volunteers at the Veterans Administration Hospital, San Francisco, by comparing the blood urate clearance values on two successive days. On the first (control) day no medication was given, but on the second zoxazolamine was administered in varying doses. The urate clearance values were paired with those for creatinine, which did not change on the successive days. The effective dosage of zoxazol-

amine was about 50 mg.; below 25 mg. the effects were inconstant. The response to 125 mg. was better than that to 50 mg. and almost as good as the response to 250 mg. Aspirin given simultaneously with zoxazolamine caused a profound fall in uricosuria; the same inhibitory effects of aspirin were demonstrated when the drug was given with probenecid and sulphinpyrazone. "Acetaminophen" (paracetamol), which has analgesic properties similar to those of aspirin, did not interfere with the action of zoxazolamine. A rise in the blood urate level has been observed in patients receiving maintenance doses of chlorothiazide; in the present study neither chlorothiazide nor hydrochlorothiazide interfered with the uricosuric effect of zoxazolamine. The uricosuric effect of the simultaneous administration of probenecid or sulphinpyrazone with zoxazolamine was roughly equal to the sum of the effects of the first two drugs. Unlike probenecid, zoxazolamine had no effect on the excretion of penicillin, phenolsulphonphthalein, or 17-ketosteroids. It has been reported that zoxazolamine given as a muscle relaxant in a dosage of 1 to 6 g. daily produces unpleasant side-effects; no such sideeffects were observed with the dosage used in this study. William Hughes

SYSTEMIC LUPUS ERYTHEMATOSUS

694. Quantitative Observations on Antinuclear Factors in Systemic Lupus Erythematosus

E. MANDEMA, V. E. POLLAK, R. M. KARK, and J. REZAIAN. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 58, 337-352, Sept., 1961. 7 figs., 40 refs.

The authors report from the University of Illinois College of Medicine, Chicago, a study of the level of antinuclear factor in patients with systemic lupus erythematosus (S.L.E.) and in their relatives. Antinuclear factor was measured by a fluorescent technique using human buccal cells, and reproducibility was good, titration of the minimum concentration of serum which gave a positive result showing variations of one tube or less in the 10 sera studied. A titre of 1:4 was regarded as positive.

None of the 40 healthy control subjects gave a reaction at a dilution of 1:4 and 33 were entirely negative, while of the 50 patients with a variety of diseases not related to S.L.E. only one gave a positive reaction. However, one or more samples of serum from 51 of the 56 patients with S.L.E. gave a positive reaction. Positive reactions were also found in the serum of 24 of the 50 relatives of these patients.

There was a general tendency for the titre of antinuclear factor to be higher in patients with clinical activity of the disease and histologically active renal lesions, but the titre was not consistently related to the serum γ -globulin level. Patients who were first observed during clinical exacerbation showed a fall in titre as their disease responded to large doses of steroids.

Two positive test results were obtained in 17 patients with rheumatoid arthritis and in 3 out of 10 patients with progressive systemic sclerosis; but in 2 patients with acute

dermatomyositis and 8 samples of serum from one patient with thrombotic thrombocytopenic purpura the results were negative.

The authors suggest that in systemic lupus erythematosus there is a breakdown of the mechanisms which normally prevent immune reactions against the patient's own tissues and they regard the occurrence of antibodies against nuclei in the relatives of patients with systemic lupus erythematosus as evidence that this abnormality is inherited.

G. L. Asherson

695. Observations on Electrophoresis of Serum Proteins from Healthy North American Caucasian and Negro Subjects and from Patients with Systemic Lupus Erythematosus

V. E. POLLAK, E. MANDEMA, A. B. DOIG, M. MOORE, and R. M. KARK. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.*] 58, 353-365, Sept., 1961. 6 figs., 13 refs.

In this further study [see Abstract 694] the authors have investigated the electrophoretic pattern of serum proteins in 49 patients with systemic lupus erythematosus (S.L.E.), observed the relation of this pattern to disease activity, proteinuria, and response to treatment with steroids, and compared it with that in 124 normal control subjects.

In the control group the negro subjects showed significantly lower levels of serum albumin and higher levels of y globulin than the white subjects (full details of the values for the serum protein fractions are given in a table). In the patients with S.L.E. the total protein value was significantly lower only in patients with proteinuria. The serum albumin level was, however, lower than normal (even in the absence of proteinuria) and was related to disease activity. A rise in the α_1 -globulin level was associated with proteinuria rather than activity, while α2-globulin levels were raised in patients with inactive disease and proteinuria. The mean β -globulin level was generally unaltered, but showed a slight decrease in patients with active disease. The y-globulin level was raised to an average of about 2 g. per 100 ml., the level being higher than normal in patients without proteinuria and lower than normal in patients with inactive disease and proteinuria. The authors graded disease activity from 0 to 3 and found that in patients without proteinuria the y-globulin level rose from Grade 0 to Grade 2, but fell slightly in the patients with Grade-3 disease activity, even in the absence of proteinuria. Patients who died within 8 weeks after the test showed lower y-globulin levels than those who survived. The ratio of albumin to y globulin correlated well with disease activity and was less affected by proteinuria than was the y-globulin value. Treatment with steroids led to a fall in the y-globulin level and a rise in the serum albumin level in individual patients, this being probably related to the control of disease activity.

The authors raise the question whether there is a hereditary difference in γ -globulin levels in white and negro subjects and emphasize the unexpected fact that the highest γ -globulin levels were found in patients with intermediate disease activity.

G. L. Asherson

Physical Medicine

696. Alcoholic Neuropathy: Its Characteristic Picture and Variants Viewed in the Light of Electromyography A. A. MARINACCI. Bulletin of the Los Angeles Neurological Society [Bull. Los Angeles neurol. Soc.] 26, 132–142, Sept., 1961. 11 refs.

After reviewing the literature on alcoholic neuropathy the author of this paper from the University of Southern California and the County Hospital, Los Angeles, discusses the aetiology and describes the electromyographic findings in some of the variants of this condition. Electromyography was carried out in a large number of cases, the findings being correlated with the clinical picture.

The cases fell into six specific groups: (1) Pure alcoholic neuritis, characterized by symmetrical denervation activity with reduction of volitional activity to discrete and usually complex motor units in the muscles of the feet and legs and, in more severe cases, in the hands and forearms also. (2) Alcoholic neuritis associated with avitaminosis, in which in addition to the changes observed in Group 1 there was evidence of generalized demyelination in the paraspinal and girdle muscles. (3) Alcoholic neuritis associated with deterioration of the arterial system, denervation activity in this group being found in the proximal limb muscles. (4) Alcoholic neuritis associated with spinal cord changes in which the denervation activity extended to the trunk and paraspinal muscles. (5) Alcoholic neuropathy associated with pressure neuropathy. (6) Pressure neuropathy incidental to alcoholic intoxication.

The clinical and electromyographic abnormalities of each group are discussed and a case characteristic of each type is described.

Kenneth Tyler

697. Prognostic Significance of Electromyography in Congenital Torticollis

C. F. BAXTER, E. W. JOHNSON, J. R. LLOYD, and H. W. CLATWORTHY JR. *Pediatrics* [*Pediatrics*] 28, 442–446, Sept., 1961. 4 figs., 2 refs.

The authors, writing from the Children's Hospital, Columbus, Ohio, describe the primary deformity in congenital torticollis as shortening of the sternocleidomastoid muscle with rotation of the head to the opposite side and flexion to the same side. The typical lesion is a firm mass in the muscle, usually noted in the first month of life. When only a small segment of the muscle is involved the mass will disappear at 5 to 6 months, but with extensive involvement permanent deformity and asymmetry occur. There is controversy concerning the need for surgical treatment of the condition, and the authors use electromyography (EMG) to help them in coming to a decision. A coaxial needle electrode is. placed in the affected muscle with an electrode on the forehead or chest. No sedation is considered necessary. The needle is placed in several locations in the muscle,

and the motor unit action potentials are recorded. The electromyograms are graded as mild, moderate, or severe according to the reduction in the amplitude and duration of motor unit activity and also the number of motor units.

Of 19 infants in whom there was extensive replacement of the muscle by a mass, 5 had virtually normal EMGs, and of these, 3 were treated conservatively and in 2 the muscle was excised. Histological examination of the excised mass showed moderate to severe scarring. All 5 cases improved. In 10 cases EMG studies showed moderate reduction in activity, and in 7 of these the muscle was completely excised. Histological examination showed moderate to severe replacement of the muscle by fibrous tissue. The 7 infants operated on had no resulting deformity and the other 3 did well. In the remaining 4 cases there was marked reduction in electrical activity and all were treated surgically. Microscopical study of the resected specimens showed extensive fibrous scarring. Two attempts to relieve the condition surgically were made in one case, but with little success. In 11 of the 13 cases treated by resection there was good correlation between the electromyographic and histological changes. The 6 cases treated with physical measures were markedly improved, with a return to normal movements: and disappearance of the mass. The duration of follow-up in these cases ranged up to . 30 months.

The authors consider that if there is severe reduction in electrical activity of the involved muscle then the deformity is likely to progress and surgical treatment is necessary; when the reduction is minimal or moderate conservative management with physical therapy is the treatment of choice.

J. B. Millard

698. Electrodiagnostic Testing in Neuromuscular Disease A. M. Rosenthal. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 829-833, Sept. 23, 1961. 13 refs.

699. The Effect of Treatment on Median Nerve Conduction in Patients with the Carpal Tunnel Syndrome H. V. GOODMAN and R. W. GILLIATT. Annals of Physical Medicine [Ann. phys. Med.] 6, 137-155, Nov., 1961. 10 figs., 10 refs.

In two groups of patients with the carpal tunnel syndrome who were treated at the Middlesex Hospital, London, either by open surgical division of the flexor retinaculum or by night splinting sensory and motor nerve conduction was studied before and after treatment. Motor nerve conduction was tested by stimulating the median nerve at the wrist with a rectangular pulse of 0·1 millisecond duration and of variable voltage up to 150 v. The response was recorded electromyographically by a

coaxial needle electrode inserted in the abductor pollicis brevis muscle and displayed on a cathode-ray oscilloscope, the stimulus being used to trigger the time-base of the oscilloscope. Sensory nerve conduction potentials were recorded from skin electrodes over the median nerve at the wrist, in response to a stimulus applied by small silver electrodes to the index finger.

A motor nerve conduction time greater than 5 msec. was considered as abnormal. In 41 of the 47 patients tested the motor conduction time was abnormal, but the delay was not always related to the clinical manifestations. Surgical division gave relief in all cases and the motor conduction latency gradually returned to normal; in the more severely affected cases, however, recovery was often slow, taking up to 2 years. Splinting cured the condition in 4 cases and improved 15 out of 25 cases. Motor nerve conduction improved in a few of these and deteriorated in others. In the sensory conduction tests a latency greater than 4 msec. and a voltage amplitude under 9 microvolts were considered abnormal. In patients on whom both motor and sensory conduction tests were performed it was found that in many cases there was no correlation between the two. The few cases in which sensory nerve conduction tests were carried out showed improvement after surgery and little change with splinting. [Some of the results are difficult to interpret.] The authors point out that motor nerve conduction tests may appear to give a normal result · owing to the response of unaffected nerve fibres, and state that sensory nerve conduction tests may provide the only indication of nerve damage. J. B. Millard

700. The Prevention of Pressure Sores: Significance of Spontaneous Bodily Movements

A. N. Exton-Smith and R. W. Sherwin. Lancet [Lancet] 2, 1124–1126, Nov. 18, 1961. 4 refs.

Holding the view that low pressures maintained for long periods are more damaging to the tissues than high pressures for short periods, the authors have studied the spontaneous movements a patient may make during the night and particularly when, for one reason or another, such movements as relieve pressure over an area "at risk" do not naturally occur. "In the normal active person the limit of tolerance to pressure is rarely exceeded; but in illness the protective mechanism may be ineffective or even abolished". Using an ingenious device (which is described on the succeeding pages of the same issue of *The Lancet*), the authors have studied the relation of the total number of spontaneous movements made by patients during sleep to the development of pressure sores.

The spontaneous nocturnal restless movements of a group of 50 elderly patients newly admitted to the Whittington Hospital, London, were individually scored on 3 to 10 consecutive nights. The patients were then grouped according to their average score into those making up to 20 movements, 21 to 50 movements, 51 to 100, and 101 and over. Of the 50 patients, whose ages ranged from 65 to 93 (average 80½ years), 10 had average nightly scores of fewer than 20 and in 9 of these pressure sores developed. One other patient had a pressure sore;

however, this patient's nightly score was only 23 and this fell progressively later on. [The authors do not say how many of the pressure sores occurred in the 14 patients who died, nor do they attempt to define the pressure sores with which they are concerned.] It is concluded that many patients make spontaneous movements during sleep which change their bodily position often enough to prevent tissue damage, and that patients whose "motility scores" during a 7-hour period at night are consistently above 20 are unlikely to get pressure sores.

In a discussion the authors state that "20% of patients newly admitted to a geriatric unit are especially at risk". [In fact, sores did develop in 20% of the present series; this is an unusually high proportion, and emphasizes the need for defining precisely what is meant by "pressure sore". The apparatus is of value because in hospitals with a shortage of nursing staff it permits selection of those patients upon whom special nursing care should be concentrated.]

P. D. Bedford

701. Trigger-point Injection: Its Place in Physical Medicine

A. L. COOPER. Archives of Physical Medicine and Rehabilitation [Arch. Phys. Med.] 42, 704-709, Oct., 1961. 3 figs., 7 refs.

It is pointed out that the "trigger-point phenomenon" is frequently encountered in the practice of physical medicine, trigger-point being defined as a "discrete area of tenderness to pressure or to stretch probably no greater than 1 mm. in radius" which produces a violent reaction to stimulation. It is a point of extreme tenderness to palpation below the skin, in the subcutaneous connective tissue, in muscle, fascia, tendon, or ligament. This phenomenon may occur in a large number of conditions and is considered by the author to be a," pathophysiologic" state rather than an anatomic abnormality; it "ceases to exist when removed for biopsy". Excessively strong stimuli may initiate a vicious circle of impulses in a network of neurones so that a chain reaction is set up. Initially, excessive afferent sensory stimuli coming into the spinal cord may create an abnormal dynamic state of the neurones of the cord and cause a "reverberating circuit" which could prolong the triggerpoint state for months or years.

Treatment must be directed to breaking the vicious circle and this can be done by accurate infiltration of the area with a local anaesthetic, by cooling sprays, or by "routine" physiotherapy. The author has treated 123 cases which had failed to respond to other measures, and claims that the results were excellent in 73%, good in 17%, and poor in 10%.

[This paper fails to convince. In tennis elbow, for example, which falls within the definition of trigger-point phenomenon, pain can also be elicited by putting the forearm extensors into tension; moreover, in a proportion of such cases (especially if the trouble is bilateral) in spite of local signs and symptoms the ultimate cause is found to lie in the cervical spine.]

D. Preiskel

Neurology and Neurosurgery

702. The Electroencephalogram in Lesions of the Inferior Brain Stem after Acute Closed Head Injury. (Электроэнцефалографическая регистрация поражений каудальных отделов ствола мозга при острой закрытой черепно-мозговой травме)

I. M. Gil'Man. Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1337-1341, No. 9, 1961. 2 figs., 7 refs.

This paper from the Hospital of the Order of Lenin, Moscow, describes the electroencephalographic (EEG) findings in 42 patients suffering from severe head injury. In all cases there was loss of consciousness, repeated vomiting, increased cerebrospinal fluid pressure, pronounced meningitic phenomena, and the clinical signs of brain-stem damage such as horizontal nystagmus, noisy rapid breathing, lability of the pulse rate, and cranial nerve lesions. Recordings were made with a 6-channel EEG machine, employing bipolar and unipolar leads.

Analysis of the recordings showed a relationship between synchronization of the EEG waves and inferior brain-stem symptoms. Clear hypersynchronization of the alpha rhythm in the posterior part of the cortex was seen more frequently in patients with moderate symptoms of inferior brain-stem damage; in those with more pronounced symptoms the alpha rhythm was less regular and less clear cut and often spread to the anterior parts of the cortex, taking the form of high-amplitude alpha -waves alternating with sharp delta waves of similar amplitude. During the process of recovery the disappearance of symptoms was paralleled firstly by greater synchronization of the alpha rhythm posteriorly, accompanied by decrease in amplitude of the waves anteriorly and then, as the occipital waves returned to a normal rhythm, by an increase in amplitude of the more anterior

Of 29 patients with a fracture of the base of the skull and signs of inferior brain-stem damage 26 showed hypersynchronization of the alpha rhythm, whereas 7 patients without inferior brain-stem symptoms showed no EEG hypersynchronization. When brain-stem symptoms were slight the hypersynchronization of the alpha rhythm was only periodic. In 4 cases there was hypersynchronization in the absence of brain-stem symptoms, but the author regards this finding as simply showing that the EEG is a sensitive index of brain-stem damage. The EEG findings should however always be considered in conjunction with the clinical picture, especially as the characteristic EEG changes may be delayed for some days.

It is concluded that the alterations in the EEG in these cases are due to disturbance of the functioning of the reticular formation which, it is postulated, is more sensitive to trauma than the specific conducting pathways.

G. P. McGovern

BRAIN AND MENINGES

703. The Effects of Hemispherectomy on Intellectual Functioning in Cases of Infantile Hemiplegia
J., McFie. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 240-249, Aug., 1961. 2 figs., 26 refs.

The author first reviews the literature on the results of hemispherectomy in infantile hemiplegia and then describes the responses to psychological testing of 34 patients subjected to hemispherectomy and of 9 in whom partial removal of damaged brain tissue was performed at the National Hospital, Queen Square, London. The patients' ages at the time of operation ranged from 1 to 31 years. Three types of lesion were present, namely, porencephalic cyst, diffuse scarring and atrophy, and unilateral Sturge-Weber disease. Comparison of the I.Os. in 28 cases treated by hemispherectomy with those in 9 who underwent partial removal showed a significant postoperative rise in intellectual level in the former group. In patients subjected to hemispherectomy, however, this increase occurred exclusively in those cases in which the brain injury was sustained before the end of the first year of life. In those in whom injury occurred after this age, intellectual loss was often seen postoperatively. In the infantile group there was no difference in the postoperative increase in I.Q. scores between patients treated by removal of the right or the left hemisphere. Most of these patients showed a verbal intellectual deficit (amounting sometimes to dysphasia), regardless of whether the right or left hemisphere had been damaged.

The author suggests that although either hemisphere can mediate many of the normal functions served by both hemispheres, there is a limit to this capacity both in time and degree.

J. B. Stanton

704. Concussion and Its Sequelae

C. SYMONDS. Lancet [Lancet] 1, 1-5, Jan. 6, 1962. 21 refs.

705. Atherosclerotic Stenosis of Cervical Arteries: Clinical Significance

J. P. WHISNANT, M. J. MARTIN, and G. P. SAYRE. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 429-432, Oct., 1961. 1 fig., 3 refs.

In a post-mortem investigation at the Mayo Clinic of the incidence of atherosclerotic stenosis of cervical arteries without symptoms of cerebral ischaemia the authors examined the aorta, the innominate artery, both subclavian arteries, the vertebral arteries up to the point where they enter the vertebral foramina, and the carotid arteries in 100 patients over the age of 50.

In 40 patients there was Grade-III or Grade-IV stenosis—that is, more than 50% obliteration of the lumen or

complete occlusion of one cervical artery. Grade-III or Grade-IV stenosis in at least one cervical artery was present in 17 (71%) of the 24 patients with symptoms consistent with cerebral ischaemia and 23 (30%) of the 76 asymptomatic patients. The differences between the two groups were quite clear, but when only the 40 cases with high-grade stenosis were considered the difference became insignificant. The percentage of patients with stenosis of the vertebral arteries was equal in the two groups, but the incidence of stenosis of the carotid arteries was higher in patients with symptoms. The relationship between stenosis of the cervical arteries proximal to the common carotid artery and vertebral arteries and the cerebral symptoms appeared to be uncertain.

The symptomatic group had a high degree of cerebral atherosclerosis, which is considered to be an important factor in the production of symptoms. The large number of asymptomatic patients with severe stenosis of a cervical artery emphasizes the need for caution in interpreting angiographic findings in relation to symptoms.

H. S. Schutta

706. Atheroma of the Carotid and Vertebral Arterial Systems

C. J. SCHWARTZ and J. R. A. MITCHELL. British Medical Journal [Brit. med. J.] 2, 1057–1063, Oct. 21, 1961. 6 figs., 10 refs.

The incidence of atheroma and stenosis of the carotid and vertebral systems was studied at the Radcliffe Infirmary, Oxford, in every 5th patient over the age of 35 coming to necropsy. The carotid and vertebral vessels were removed from 93 such patients and examined in detail by 2 observers. Severe atheroma was found most frequently in the carotid sinus, which was often calcified and ulcerated; in one subject in 7 severe stenosis was present. The terminal carotid segments often showed calcified plaques. The vertebral arteries, although less severely affected by atheroma than the carotid arteries, were often stenosed because of their small bore. Analysis of the sites and grades of lesions in the various age groups and in the two sexes showed frequent striking differences in the sites of stenosis in different vessels. Proximal lesions appeared to be common in vessels arising at right angles from the parent vessel and lesions seemed to be particularly common at the site of turbulence; it is suggested that dynamic factors due to blood flow probably play an important part in the production of vascular lesions. The practical importance (from the point of view of angiography) of the frequency of lesions in the innominate, subclavian, and common carotid arteries is emphasized. -

Narrowing at some point in the vertebral or carotid arteries was found in 90% of the males and 85% of the females; in about half of these it was severe, and narrowing at one site was likely to be associated with narrowing at another. Because of the importance of the carotid sinuses, the authors examined the sinuses from 293 consecutive and unselected patients coming to necropsy. It was found that if one sinus was not stenosed there was an 81% chance that the other would also be free from stenosis, but if one was severely stenosed there was only a

19% chance that the other would be free. The incidence of strokes and the incidence of arterial disease increase with age. The authors state, however, that without further evidence it should not necessarily be concluded that "the stroke is caused by the narrowing".

R. B. Thompson

707. Cerebrovascular Disease: IX. The Medullary Blood Supply and the Lateral Medullary Syndrome A. B. Baker. Neurology [Neurology (Minneap.)] 11,

852-861, Oct., 1961. 5 figs., 36 refs.

The author doubts the correctness of the traditional ascription of the lateral medullary syndrome to occlusion of the posterior inferior cerebellar artery. Accordingly, at the University of Minnesota, Minneapolis, he has carried out an anatomical and pathological study of the medullary blood supply in a series of 275 brains taken from patients who had not suffered from bulbar symptoms. In 26% of these specimens the posterior inferior cerebellar artery was absent on one or both sides, and the lateral medullary region was supplied by small vessels arising directly from the vertebral artery. Even when the posterior inferior cerebellar artery was present it made only a small contribution to the blood supply of the lateral medullary region, which was mainly nourished directly by branches of the vertebral artery. The posterior inferior cerebellar artery, unlike the vertebral artery, was very seldom significantly narrowed by atherosclerosis.

In 16 patients (6% of the series) there was discovered a combination of severe atherosclerosis of the vertebral artery and absence of the posterior inferior cerebellar artery, though there had been no history of signs of bulbar insufficiency in these cases. Such patients are thought to be in constant jeopardy, since any incident diminishing the vertebral circulation, such as a fall in blood pressure, an abrupt change in head position, or the injection of contrast medium for angiography, might precipitate the lateral medullary syndrome. In the author's experience 3% of all patients over the age of 60 have severe atherosclerotic narrowing of one or both vertebral arteries, and this fact accounts for the numerous complications of vertebral angiography in this age group, and for the frequent occurrence of bulbar symptoms related to changes of head position.

Bernard Isaacs

708. Paroxysmal Symptoms in Intracranial Hypertension, Studied with Ventricular Fluid Pressure Recording and Electroencephalography

D. H. INGVAR and N. LUNDBERG. Brain [Brain] 84, 456-469, Sept., 1961. 4 figs., 20 refs.

At the University of Lund, Sweden, the authors have simultaneously recorded the electroencephalogram (EEG) and intraventricular fluid pressure (V.F.P.) over prolonged periods in 6 patients suffering from raised intracranial pressure, this being due in 5 cases to an intracranial tumour and in one to diffuse carcinomatosis of the meninges.

The resting EEGs showed bilateral slow wave activity accentuated on the side of the tumour. The resting V.F.P. was increased and two types of V.F.P. wave

could be distinguished. The first type, or "plateau waves", lasted about 40 minutes, during which the V.F.P. rose to 100 mm. Hg, this being accompanied clinically by restlessness, confusion, and later loss of consciousness, with clonic movements of the limbs and tonic flexor rigidity; the severity of these symptoms was related to the height of the V.F.P. The EEG during these episodes was either unchanged or showed arousal phenomena. No cortical epileptic discharges accompanied the seizures. On one occasion only did the EEG show an increase of slow activity with increased V.F.P. It was not possible to determine whether the arousal phenomena were preceded or followed by the rise in V.F.P. Spontaneous or voluntary hyperventilation lowered the V.F.P. to 0 to 5 mm. Hg, and this was accompanied by an increase in the slow components in the EEG. The second type of V.F.P. wave was of the rhythmic "1-per-minute" type described by Lundberg; the rise in V.F.P. appeared during drowsiness, being synchronous with periodic breathing and accompanied by arousal effects in the EEG.

The mechanism of the seizures during raised V.F.P. is discussed and it is suggested that they arise subcortically from structures which are either transiently disconnected from the cortex or have no effect on cortical activity. It is possible that the V.F.P. waves are initiated by vasomotor changes.

H. S. Schutta

709. Obstruction of the Foramina of Luschka and Magendie. (L'obstruction des trous de Luschka et de Magendie)

M. DAVID, A. DJAHANCHAHI, and J. ABOULKER. Neuro-chirurgle [Neuro-chirurgle] 7, 210-227, July-Sept., 1961. 10 figs.

In this communication 5 cases of obstruction to the outflow from the fourth ventricle, operated on at the Hôpital Saint-Anne, Paris, are fully reported and a further 23 cases from the literature are analysed. Of the authors' 5 cases 2 were in infants who presented with hydrocephalus and proved to have agenesis of the vermis with atresia of the foramina. One died 24 hours after operative relief of the obstruction, but the second survived operation. The other 3 patients were adults who presented primarily the features of raised intracranial pressure and to a lesser extent showed localizing signs suggesting lesions either in the posterior fossa or in the hypophysial region. At operation the vermis was incised and (in 2 cases) the amygdala removed. Postoperatively all 3 patients made a complete recovery.

The authors claim that the diagnosis of obstruction of the foramina of Luschka and Magendie can be made preoperatively (and indeed was so in 3 out of their 5 cases). For this purpose they present a comprehensive account of the clinical and radiological features of the condition. Radiographs of the skull show the signs of raised intracranial tension; air encephalography does not fill the ventricles or the intracranial part of the cisterna magna; the amygdala were not seen in the cases with agenesis of the vermis, and in the other cases they were below the foramen magnum. Ventriculography reveals dilatation of the entire ventricular system; air does not enter the cisterna magna or the subarachnoid space. In agenesis

of the vermis air in the fourth ventricle extends to the occipital bone posteriorly, whereas in the other cases a significant layer of tissue intervenes. The authors conclude by emphasizing the good postoperative prognosis in cases with normal cerebellar morphology, and also their uncertainty about the best treatment of cases with agenesis of the vermis.

B. S. Meldrum

710. Pneumococcal Meningitis in the Adult: Clinical, Therapeutic, and Prognostic Aspects in Forty-three Patients

R. A. Olsson, J. C. Kirby, and M. J. Romansky. Annals of Internal Medicine [Ann. intern. Med.] 55, 545-549, Oct. [received Dec.], 1961. 2 figs., 5 refs.

The authors review their experience of pneumococcal meningitis in 43 adults seen at the District of Columbia General Hospital, Washington; between 1950 and the end of 1960. Of 23 patients given intramuscular or intravenous injections of penicillin 12 (52%) died. Of 7 who received penicillin and one of the tetracyclines intravenously 6 (85%) died, and of 6/given erythromycin intravenously 3 (50%) died. The authors state that in the remaining 7 patients there was "a wide variety in forms of therapy". The over-all mortality in this series of 43 patients was 65%.

[A review of other series of cases of pneumococcal meningitis reported in the literature has shown that treatment with a combination of intrathecal and intramuscular injections of penicillin is often more effective than treatment with intravenous or intramuscular injections alone. The authors do not refer to the efficacy of treatment with a combination of intrathecal and systemic administration of penicillin, and it appears that none of their 43 patients received penicillin intrathecally.]

A. G. Freeman

711. Mental Deterioration in Epileptic Children

M. R. CHAUDHRY and D. A. POND. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 213-219, Aug., 1961. 1 fig., 8 refs.

In this comparative study, undertaken to elucidate the factors apparently related to mental deterioration in epileptics, 28 epileptic children from the Maudsley and Fountain Hospitals, London, who showed mental and social deterioration were compared with an equal number of epileptics matched for age and sex with similar evidence of brain damage but not of mental deterioration. Idiot or imbecile children with congenitally impaired intelligence were not included, nor were cases of the well recognized neurological degenerations such as occur in the lipidoses.

The investigation revealed the comparative lack ofimportance in the production of deterioration of such factors as (1) the age at which brain damage occurred; (2) the number of years during which the fits had continued; (3) the quantity of anticonvulsant drugs used; and (4) associated emotional and behavioural problems. In contrast the close correlation between mental deterioration and the number and frequency of epileptic attacks, and also the apparent reversibility of deterioration when the attacks had been brought under control was striking in certain cases. In view of these findings the authors suggest that some form of subclinical epilepsy in some cases may cause apparent deterioration which, however, is not a true dementia.

J. B. Stanton

712. Epilepsy Due to Small Focal Temporal Lesions with Bilateral Independent Spike-discharging Foci: a Study of Seven Cases Relieved by Operation

M. A. FALCONER and W. A. KENNEDY. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 205–212, Aug., 1961., 6 figs., 14 refs.

From the Maudsley Hospital, London, the case histories are presented of 7 patients with long-standing temporal lobe epilepsy refractory to medical treatment whose electroencephalograms (EEGs) showed bilateral, apparently independent, foci in the temporal regions. All these patients were subjected to unilateral temporal lobectomy; this resulted in subsequent cure or considerable improvement in the epilepsy and the ultimate disappearance of spike discharges on both sides. In each case a symptomatic cause for the epilepsy—glioma, hamartoma, angioma, or meningioma—was revealed in the removed temporal lobe.

The authors draw attention to the postoperative decline, and eventual disappearance, of the seemingly independent spike focus on the unoperated side. Selection of the correct side for lobectomy in such cases can be difficult and all the evidence, clinical, radiological, and that derived from EEG recordings has to be weighed. From the EEG point of view unilateral slow activity and diminution of barbiturate-induced fast activity may be helpful guides in deciding on which side the causative lesion is situated.

J. B. Stanton

713. The Incidence of Temporal Lobe Epilepsy among a Hospital Population of Long-stay Female Epileptics J. H. Margerison and D. W. Liddell. Journal of Mental Science [J. ment. Sci.] 107, 909-920, Sept. [received Nov.], 1961. 3 figs., 28 refs.

In the study here reported from Runwell Hospital, Essex, the entire patient population of St. Faith's Hospital, Brentwood, consisting of 270 female epileptics was surveyed in order to assess the incidence of temporal lobe epilepsy, the investigation being made both clinically and by study of the electroencephalograms (EEGs). The two assessments were made separately, the EEGs being coded by number to prevent recognition.

In the final clinical assessment, which was made on 204 patients, both clinicians agreed that 159 (77.9%) were cases of temporal lobe epilepsy, that 23 were not temporal lobe cases, and they disagreed on 22 cases. Classification on the basis of the EEG recordings, using Bingley's criteria, gave the incidence of temporal lobe epilepsy as 74.5%. When the incidence was computed on both the clinical and EEG findings the figure was reduced to 60.8%. Finally if the criterion of a localized reduction in barbiturate-induced fast activity in the EEG between the sphenoidal and mid-temporal electrodes was considered together with the other methods the incidence fell to 33.8%, a figure which agrees closely with the inci-

dence of temporal lobe lesions in patients coming to necropsy.

The value of this type of strict classification is discussed and it is suggested that greater correlation between the EEG and neuropathological findings is desirable. The importance of this is emphasized in relation to the question of lobectomy in the surgical treatment of temporal lobe epilepsy.

E. H. Johnson

714. Crises in Post-encephalitic Parkinsonism G. Onuaguluchi. Brain [Brain] 84, 395-414, Sept., 1961. 3 figs., 27 refs.

In a study at Stobbill General Hospital, Glasgow, of 67 patients suffering from postencephalitic Parkinsonism the author found that in addition to oculogyric crises, there may be crises of sweating and of "breath-holding". In 8 patients there were paroxysmal attacks of excessive sweating even in the winter months, with flushing of the face and at times conjunctival congestion and also tachycardia. The clinical manifestations of oculogyric crises are described in detail and it is noted that they are frequently accompanied by nystagmus. Discussing the pathogenesis of oculogyric crises the author suggests that the deviation of the eyes is the result of a vestibuloocular reflex in patients with brain-stem lesions involving the vestibular pathways and that the emotional changes which so often accompany the crises are probably the result of stimulation of the diencephalon.

J. W. Aldren Turner

715. Parkinson's Syndrome. [Review Article] A. C. ENGLAND JR. and R. S. SCHWAB. New England Journal of Medicine [New Engl. J. Med.] 265, 785-792, Oct. 19, 1961, and 837-844, Oct. 26, 1961. 8 figs., bibliography.

SPINAL CORD

716. Angiographic Study of the Circulation of the Lower Limbs at Different Evolutive Stages of Paraplegia. (Étude angiographique de la circulation des membres inférieurs aux différents stades évolutifs d'une paraplégie)

P. GALIBERT, P. FOSSATI, C. LOPEZ, J. P. CÉCILLE, G. BONTE, P. DECOULX, and E. LAINE. *Neuro-chirurgie* [*Neuro-chirurgie*] 7, 181–201, July–Sept., 1961. 7 figs., 23 refs.

The authors, working at the Centre Hospitalier Régional, Lille, have studied angiographically the lower limbs of 31 patients with paraplegia (25 with traumatic spinal lesions and 6 with compression by a tumour) in order to assess the role of the arterio-venous anastomoses in the "arterialization" of the venous blood which Claude Bernard observed to follow spinal transection. Radiographs of the entire leg were taken at the end of the 5 seconds required for the retrograde injection of 25 ml. of contrast medium into the femoral artery and repeated at 5-second intervals during the subsequent 25 seconds. Objective confirmation of the timing was provided by a clock included in the radiographic field. In 5 cases

patients were studied early in their illness and again after recovery or progression.

The angiogram was considered to be normal in 11 patients. Abnormal angiograms showed the following features: (1) excessively rapid arterial filling, the plantar arteries being seen on the first film; (2) premature venous return, either proximal or distal; if proximal, the veins of the thigh were visible on the second film, and if distal, arterio-venous anastomoses were visible in the plantar region and the saphenous veins were sharply defined on the second film. Patients with actual or impending trophic lesions always showed a premature venous return. Of 11 patients with total flaccid paraplegia 8 showed premature venous return; the other 3 were receiving ephedrine and adrenaline as therapy for hypotension and bradycardia.

The results are discussed in the light of the classic studies of Grant and Blond (Heart [now Clin. Scl.], 1930, 15, 281 and 385). It is concluded that the premature venous return in the legs of paraplegics is a consequence of the interruption of the sympathetic supply to the arterio-venous anastomoses. When present, premature venous return suggests the need for extra nursing care to prevent trophic lesions.

[Although the authors present an admirable tabulation of the findings in the 31 patients, this does not substantiate the relationship claimed between premature venous return and trophic lesions, for in 5 of the 16 patients with lesions present or impending, the angiograms were normal.]

B. S. Meldrum

DISSEMINATED SCLEROSIS

717. The Benign Form of Multiple Sclerosis. A Study Based on 241 Cases Seen within Three Years of Onset and Followed up until the Tenth Year or More of the Disease

D. McAlpine. *Brain* [*Brain*] **84**, 186-203, June [received Aug.], 1961. 2 figs., 17 refs.

The present study is based on a prospective follow-up of 241 patients who attended the Middlesex Hospital. London, and in whom the original diagnosis was multiple (disseminated) sclerosis. The series was limited to those patients whose disease began between January, 1930, and December, 1949, and who were seen during the first 3 years of the disease. The follow-up terminated in November-December, 1959. In analysing the final results the classification was dead, 83 patients; disabled, 80 patients; and unrestricted, 78 patients. The results of an analysis of the degree of disability in 80 patients show that of those followed up for 15 to 20 years a significant proportion were not severely incapacitated. Seventy-eight patients, or roughly one-third of the whole series, at the end of the follow-up period were without restriction for normal employment and domestic life but were not necessarily symptom-free. In 46 of these patients the diagnosis was "definite", in 20 "probable", and in 12 "possible". With the exception of 4 patients, those in the first 2 categories were personally examined at the end of 1959.

Twenty-three patients had no relapse after the first year; 14 of these were classified as "probable" and 9 as "possible". In the remaining 55 patients the average annual relapse rate was at its height in the first 2 years. Between the 3rd and 10th years the rate fell by twothirds and after the 10th year it further declined. The incidence of lower limb weakness, as an initial symptom, in the dead and disabled groups was roughly double that in the unrestricted group, whereas unsteadiness in walking (of cerebellar origin) occurred with approximately the same frequency in the 3 groups. In 163 patients comprising the dead and disabled, the incidence of unilateral or bilateral extensor plantar responses within 3 years of onset was 70% compared with the figure of 38% in the unrestricted group. Of the 83 patients who had died, 54% were moderately or severely paraplegic when first seen. Cerebellar signs were present in 41% of patients in the dead and disabled groups at the initial examination, contrasting with 14% in those patients in the unrestricted group. These findings suggest that if a patient within 3 years of the onset of multiple sclerosis shows signs of an established paraplegia, especially when accompanied by cerebellar ataxia, disability is likely to increase in severity, subsequent relapses enhancing this risk and increasing the probability of premature death.

The exceptionally high percentage of patients in this series in whom the disease appears to be running a mild course can partly be explained by the inclusion of 23 among the probable and possible cases who, so far, have not relapsed after the first year. Reasons are given for the belief that these and the remaining cases in the unrestricted group represent a benign form of multiple sclerosis. The alternative possibility that a "primary" or "spontaneous" form of acute disseminated encephalomyelitis accounted for the original symptoms only arose in 2 cases. Furthermore, doubt is expressed as to the existence of this form of acute disseminated encephalomyelitis as a clinical entity. The main characteristics of the benign form of multiple sclerosis appear to be as follows-first, an acute type of onset affecting optic nerve, brain stem or dorsal columns of the spinal cord; secondly, a low relapse rate, particularly after the 2nd year, and thirdly when relapses do occur their effect on pyramidal and cerebellar pathways is relatively slight's and transient. If, in a particular patient, these conditions still hold after the disease has been in existence for 10 years, the prognosis is quite favourable, bearing in mind that exceptionally a severe relapse leading to disability may occur late in the disease.

A brief reference is made to treatment. The period of rest in the early active stage of the disease, the advice given as to future mode of living and the stress laid on rest in bed during a relapse may have played a part in modifying the course of the disease. Treatment with intravenous "novarsenobillon" [neoarsphenamine], usually preceded by artificial fever, and followed by liquor arsenicalis between the courses, was carried out in 46 patients for a minimum of 2 years. Statistically the value of this treatment is not apparent although the possibility cannot be dismissed that in some patients it may have contributed to the subsequent freedom from serious relapse.—[From the author's summary.]

Psychiatry

718. Psychiatric Illness in Adolescence: Presentation and Prognosis

P. T. Annesley. Journal of Mental Science [J. ment. Sci.] 107, 268-278, March [received Aug.], 1961.

This paper reviews 362 patients admitted to the adolescent unit at St. Ebba's Hospital, Epsom, between 1949 and 1954 and followed up for over 2 years. Behaviour disorder accounted for half the admissions. The prognosis was good in comparison with the adult psychopath, 38% making a complete remission. The most valuable guide to prognosis was the symptomatology. Stealing as an isolated symptom had an excellent outcome whilst a combination of stealing, violence, and truancy in the same individual was of poor import. Heredity and background showed little relationship to prognosis.

A quarter of admissions suffered from schizophrenia with symptoms similar to those in adult life. The prognosis was poorer than in adults, only a fifth recovering compared with a third of adults. Heredity and background had little influence on outcome. The most significant prognostic factor was sex, twice as many females making a complete remission. Results were similar with deep insulin and psychotherapy. A quarter of patients suffered from neuroses and affective disorders. Obsessional states and affective psychoses were rare, each forming 2% of admissions, and their prognoses were excellent.

Schizophrenia developed in a few patients originally placed in other diagnostic categories. This was most common with anxiety states (15%), less with hysteria (7%), and rare in behaviour disorders (1%). No patients with obsessional states or affective disorders developed schizophrenia at follow-up.—[Author's summary.]

719. The Reliability of Psychiatric Assessment: an Analysis

N. Krettman, P. Sainsbury, J. Morrissey, J. Towers, and J. Scrivener. *Journal of Mental Science [J. ment. Sci.*] 107, 887–908, Sept. [received Nov.], 1961. 7 refs.

Six groups of patients, each of 15 new referrals to the Chichester Mental Health Service, were independently examined by pairs of psychiatrists at approximately 3-day intervals. The groups were homogeneous with respect to age, sex and social class.

Agreement on duration of present illness was attained in about 60% of patients, being lowest for the patients diagnosed as neurotic. Agreement on family history was obtained in about 85% of patients, being lowest with those over 55 years of age. Agreement on previous psychiatric illness was reached in about 70% of patients with higher agreement among those diagnosed as having an organic illness. On comparing the assessments made on symptomatology, agreement values of between 85% (for depression) and 0% (for aggression, thought-disorder) were found. The final rank order correlated at a

significant level with that for the incidence of the various symptoms.

Agreement on diagnosis, using an agreed list of 11 possible diagnoses, was attained at a specific level in about 65% of the patients and at a broader or generic level in a further 15%. Agreement on diagnosis was strongly associated with agreement on previous history and with the number of previous illnesses. On the other hand there was no demonstrable association with agreement on symptoms or with the other variables mentioned. Highly significant discrepancies emerged between the agreement levels achieved in different diagnostic categories, being highest with organic patients and lowest with neurotics.

Agreement on therapy (based on a choice of 10 treatments) was found in 65% of the cases, with approximate agreement in a further 5%. The level was considerably higher in the functional psychoses than in the remaining patients and in the former group it was also shown that agreement on therapy reflected diagnostic agreement, though this association could not be substantiated for the total sample. It was also shown that diagnosis had significant inferences for therapy. E.C.T. [electric convulsion therapy] and psychotherapy were recommended with a far higher level of concordance (each about 75%) than was pharmacological therapy (40%).

No important differences could be demonstrated between the ability of the 5 psychiatrists taking part in reaching agreement with their colleagues on any of the variables enumerated above. Comparison of our findings with those of other workers confirms that concordance of diagnostic opinion varies according to the diagnostic group and also suggests that higher levels are attained with more severely disturbed patients.—[Authors' summary.]

720. Cycloid Psychoses—Endogenous Psychoses which are neither Schizophrenic nor Manic-depressive

K. LEONHARD. Journal of Mental Science [J. ment. Sci.] 107, 633-648, July [received Sept.], 1961. 8 figs., 5 refs.

The concept of the cycloid psychoses was introduced by Kleist, who described a motility psychosis and a confusion psychosis; the concept was later rejected by its founder, but developed and extended by the present author as described in this paper. The acute recoverable functional psychoses, which according to the latter are neither manic-depressive nor schizophrenic, are stated to form an entity characterized by presenting two contrasting clinical states at different times, and by complete remission with no residual defect even after repeated attacks. He describes three subgroups: (1) motility psychosis, characterized by phases of hyperkinesia involving reactive and expressive movements representing quantitative changes in psychomotor activity, and by phases of akinesia; (2) confusion psychosis,

in which there are an excited phase with pressure of talk and misidentifications and an inhibited phase in which mutism, stupor or semi-stupor, perplexity, and ideas of reference are associated; and (3) anxiety-elation psychosis, in which morbid anxiety and ideas of reference may alternate with expansiveness and elation.

A case history of each kind of illness is cited and the clinical pictures characteristic of each of the groups are described. Whilst this group of cycloid psychoses is stated to be distinct from other functional psychoses, admixtures frequently occur between features of the three subgroups. They may also be difficult to distinguish respectively from periodic catatonia, schizophasia, and affect-laden paraphrenia, all of which belong to the author's non-systematic group of schizophrenias, distinguished from the so-called nuclear group by their clinical features and their better prognosis.

. R. H. Cawley

721. Posthypnotic Stimulation of Hypnotically Induced Conflict in Relation to Psychosomatic Reactions and Psychopathology

J. REYHER. Psychosomatic Medicine [Psychosom. Med.] 23, 384-391, Sept.-Oct., 1961. 3 refs.

The author describes a study in which the psychic and somatic responses to a contrived psychological situation were observed. The technique involved the subsequent evocation of a conflict induced under hypnosis.

A hostility-laden situation was communicated to 11 normal adult subjects under deep hypnosis. Two separate conflicts were conveyed, one being intended to provoke a greater sense of guilt than the other. Subsequent tachistoscopic testing was carried out by means of presenting critical and neutral words with reference to the conflict situation in a modified ascending series of exposure times. An objective index of the degree of repression of conflict was constructed mathematically. It was found that the degree of repression correlated well (r=0.74) with the proportion of somatic reactions to the recognition of critical words.

The symptoms were divided into 13 categories, 7 of which consisted of various types of somatic response. The degree of repression was held to be significant in determining the posthypnotic reactions. The latter could not be comprehended in terms of shift of attention.

A. Balfour Sclare

722. Children who Starve Themselves: Anorexia Nervosa

J. R. BLITZER, N. ROLLINS, and A. BLACKWELL. *Psychosomatic Medicine [Psychosom. Med.]* 23, 369–383, Sept.—Oct., 1961. 1 fig., 22 refs.

A clinical study of 15 children (12 female and 3 male, aged 7 to 14 years) suffering from anorexia nervosa is reported from the Children's Hospital Medical Center, Boston. Most of the children denied the existence of their obvious emaciation, but a number of them expressed animistic ideas about food. Open conflict between the mothers and grandmothers of the children was a prominent factor during the infancy of many of the patients who often re-created this conflict with their own mothers,

"using food as the bone of contention". There was a high degree of anxiety concerning menstrual function among the affected girls. Depression was present in 13 patients, but was not accompanied by self-depreciation. In addition, pronounced regression to an infantile state of dependency was characteristic, and was often exacerbated by parental over-protection. Of the 15 patients, 9 recovered, one died, and 5 continued to have some degree of eating disorder. Patients with hysterical personality traits fared particularly well, and progress appeared to be made where a disturbed parent—child relationship could be favourably influenced by psychotherapy to the parents and the child.

A. Balfour Sclare

723. Impramine (Tofranil) in Depressive States: a Controlled Trial with In-patients

C. FRIEDMAN, M. S. DE MOWBRAY, and V. HAMILTON. *Journal of Mental Science [J. ment. Sci.*] 107, 948-953, Sept. [received Nov.], 1961. 6 refs.

This paper reports a controlled trial carried out on 50 in-patients at Springfield (Mental) Hospital, London, suffering from depression and treated with "tofranil" (imipramine), consecutively admitted cases being randomly allocated to the treatment group or a placebo group. Each patient was assessed by interview, each completed a questionary, and in addition, was separately rated on two scales. The usual duration of treatment was 6 weeks; at the final analysis 36 cases were available for evaluation.

Of the 17 patients given imipramine 11 showed improvement, compared with only 4 of the 19 receiving the placebo. Endogenous and involutional depression responded better than did reactive depression. It is noted that 8 of the most severely ill patients in this series did not respond to imipramine, although 5 of them subsequently improved after electric convulsion therapy (E.C.T.). A number of side-effects developed during the first few days of treatment with imipramine, but soon receded. It is concluded that imipramine is of value in the treatment of less severe depressions, but in severe cases would appear to be inferior to E.C.T.

E. H. Johnson

724. Salivary Secretion in Depressive Illness

B. M. DAVIES and J. B. GURLAND. Journal of Psychosomatic Research [J. psychosom. Res.] 5, 269-271, Oct., 1961. 6 refs.

At the Bethlem Royal Hospital, London, tests of salivary secretion were carried out on 30 patients with primary depressive illness, 11 patients with schizophrenic illness of recent onset, and, for purposes of control, 25 members of the nursing and occupational therapy staff, all the patients and controls being females. The test was carried out in the morning, no food, drink, or sweets being allowed for one hour beforehand. Except for the usual night sedative all drugs were withdrawn for the preceding 24 hours. Dental cotton rolls 4×2 cm. in size, which were used to absorb the saliva, were placed on each side of the mouth against the parotid duct and under the tongue, and were left in situ for 2 minutes. They were then placed in waxed cardboard

sputum cups, the difference in weight before and after use giving the weight of saliva produced. It was found that depressed schizophrenic patients secreted significantly less saliva than healthy subjects. The tests were repeated on the same subjects after salivary stimulation with two drops of syrup of lemon extract placed on the tongue. After stimulation the schizophrenic patients produced significantly less saliva than the other groups and the depressives, in turn, produced significantly less than normal subjects. The use of salivary secretion as a physiological index of autonomic activity is discussed and further studies are suggested.

J. B. Stanton

725. Environmental and Hereditary Factors in the Schizophrenias of Old Age ("Late Paraphrenia") and their Bearing on the General Problem of Causation in Schizophrenia

D. W. K. KAY and M. ROTH. Journal of Mental Science [J. ment. Sci.] 107, 649-681, July [received Sept.], 1961.

The authors include in the category of "late paraphrenia" all patients aged 60 and over having a paranoid symptom complex without signs of organic cerebral pathology and in whom illnesses were judged from their content not to be primary affective disorders. They report a study of 99 such patients, 42 admitted to Graylingwell Hospital, Chichester, in 1951–5, and 57 admitted to the Psychiatric Hospital, Stockholm, in 1931–40. Clinical records, family histories, and follow-up data were examined, and groups of patients of similar age admitted with affective and organic disorders over the same periods were used for comparison.

Both paraphrenic groups showed similar characteristics. There was a significant excess of females over males (7:1); unmarried patients were more common than in the general population of similar age, and married patients had fewer children. Significantly more paraphrenics were living alone than were patients with affective-disorder; and of those living alone, more of the paraphrenics were socially isolated, mainly because of having few surviving relatives, because of deafness, or through having had long-standing abnormalities of personality. The clinical picture was characterized by many schizophrenic symptoms; disorders of thought, mood, and volition were conspicuous, as were hallucinations. Intellect, personality, and memory were unimpaired as a rule. Three clinical varieties are tentatively defined: (1) abnormal personalities developing paranoid psychoses, without hallucinosis; (2) paraphrenias arising in adverse circumstances or after prolonged isolation; and (3) mainly endogenous paraphrenias.

The authors discuss aetiology and outcome in detail; the course is generally chronic, cerebral degeneration of a pathological degree is rare, and the expectation of life is only slightly reduced. They conclude that late paraphrenia is the manifestation of schizophrenia in later life, and that aetiological considerations have some bearing on problems of aetiology of schizophrenia in general. Genetic factors are likely to be of less importance than for schizophrenia in early life; social isolation and situational stress may arise because of personality devia-

tions or more fortuitously, and the normal cerebral degenerative processes may also contribute to the onset of illness in later life.

R. H. Cawley

726. Orosomucoid in Schizophrenia

M. GOODMAN, E. D. LUBY, C. E. FROHMAN, and J. S. GOTTLIEB. *Nature* [*Nature* (*Lond.*)] 192, 370–371, Oct. 28, 1961. 6 refs.

Orosomucoid is an apparently homogenous serum glycoprotein the serum levels of which have been found to be elevated in a number of conditions, particularly in states of advanced malignancy (Goodman et al., J. Lab. clin. Med., 1957, 50, 758). A raised serum orosomucoid level is accompanied by a serum albumin level which is lower than normal. In the study here briefly reported from Wayne State University College of Medicine, Detroit, the serum levels of these proteins in 40 cases of chronic schizophrenia were determined and compared with those in 41 non-psychotic control subjects (laboratory personnel). In both groups the subjects were not taking drugs, were free from physical disease, and in two-thirds of the patients the diet was controlled. Serum levels of orosomucoid and albumin were determined by immunochemical methods involving the precipitin reactions of specific chicken antisera.

The mean serum albumin value for the schizophrenic group was 45.7 ± 4.5 mg. per ml. and for the control group 48.3 ± 3.4 mg. per ml. (P<0.01), while the mean serum orosomucoid values were 1.005±0.196 mg. per ml. in the patients and 0.842±0.185 mg, per ml. in the controls (P<0.001). The serum albumin: orosomucoid ratio was also significantly different in the two groups, being 0.0223 and 0.0175 respectively. The interpretation of these results is necessarily tentative. The authors suggest that in organic conditions the serum orosomucoid level may be raised either as a result of processes destructive of tissue, presumably through release into the blood stream of tissue glycoproteins, or through non-specific stress mechanisms. In schizophrenia it is suggested that orosomucoid may be a reactor to various non-specific stressors not necessarily associated with organic changes. R. Rodnight

TREATMENT

727. The Treatment of Prolonged Insulin Coma W. W. KAY. *Journal of Mental Science [J. ment. Sci.*] 107, 194–232, March [received Aug.], 1961. 8 figs., 39 refs.

The author describes the treatment with cortisone and ACTH (corticotrophin) of prolonged coma occurring in the course of deep insulin coma therapy on the basis of 55 out of 62 cases collected over 3½ years from 13 hospitals. All the cases had failed to respond to the usual methods of treatment; the latter are described, together with the biochemistry of normal insulin coma. Factors in the aetiology of prolonged coma are stated to include vitamin-B deficiency, water loss, failure to maintain carbohydrate intake, sensitization to insulin, and the formation of loculi of insulin.

The patients were assessed clinically, and full laboratory investigations-including estimation of blood glucose, electrolyte, and protein levels, and determination of blood count, haemoglobin concentration, and packed cell volume-were carried out, and repeated as required. Adequate amounts of mixed B vitamins were given as a routine, and 331% glucose in saline was injected intravenously if there was hypoglycaemia, Cortisone or ACTH, 50 mg., was administered intramuscularly, and a further injection given after an hour where necessary. Some patients received both hormones. Intragastric feeding was instituted when recovery had not occurred after half an hour, the feeds containing water, glucose, potassium chloride, and sodium bicarbonate. If recovery had not taken place by the second day intragastric feeding of citrated milk was begun. Penicillin was given from the start. Cardiovascular collapse was anticipated and dealt with early.

Of the 55 patients, 12 responded within an hour of receiving hormone treatment, 10 recovered within a few hours, and 18 by the next day; 8 took some days but less than a week, and 3 took more than a week. Four patients died, and the post-mortem findings are discussed.

The author concludes that fatigue of the anteriorpituitary-adrenocortical system and disturbance of the vitamin-B coenzyme system are important factors in the aetiology of prolonged insulin coma. The administration of cortisone or ACTH, after raising the blood glucose level to normal; helps to rouse the patient as well as stabilize the blood glucose level. Recovery is not affected by the dose of insulin used to induce coma, nor by the interval between the onset of coma and administration-of the hormone up to about 9 hours. Prolonged coma tends to occur early in the course of insulin coma therapy, and patients who receive a second or third course are likely subjects. Death when it occurs is due to collapse, exhaustion, or pneumonia. The author considers that treatment with cortisone and ACTH is a useful advance on previous methods. In the present series cortisone appeared to be slightly more effective than ACTH, but it is pointed out that ACTH gel (long-acting) is now available and " is useful to give slow, continuous stimulation of the adrenal cortex when the first dose of hormone fails to rouse the patient in 3 to 4 hours".

J. S. Bearcroft

728. Study of Esucos (U.C.B. 3412) in a Group of 91 Psychotic and Neurotic Patients. (Étude de l'esucos ou U.C.B. 3412 chez un groupe de 91 malades psychotiques et névrotiques).

J. PAQUAY, F. ARNOULD, P. BURTON, M. TINANT, and E. MOTTET: Acta neurologica et psychiatrica Belgica [Acta neurol. belg.] 61, 686-696, Aug. [received Oct.], 1961. 5 refs.

"Dixyrazine" ("esucos"), a drug combining a phenothiazine nucleus and the right hand chain of atarax or hydroxyzine, was given to 91 psychiatric patients, of whom 35 were hospital in-patients and 56 were private out-patients, in a dosage varying from 30 to 300 mg. per day; the drug was combined in some cases with imipramine or other antidepressive drugs. Side-effects,

which occurred particularly when the dose exceeded 50 mg. per day, included an increase in body weight, seborrhoea, discoloration and puffiness of the skin with loss of elasticity, thinning of the hair, a tendency to baldness, an increase in muscular tone, and somnolence. The patients were followed for up to 10 months.

Among the in-patients, most of whom were schizophrenics, the effect of the drug was largely sedative and only patients who had a diagnosis of character disorder and psychasthenia gained some benefit. Of the outpatients, who were suffering variously from hypochondriasis, anxiety states, and depressive illnesses, dramatic improvement occurred in more than one-third, the drug being particularly effective in the reactive depressions. The authors conclude that dixyrazine has an undoubted clinical effect, which is most apparent in the psychoneurotic disturbances. In a double-blind trial on 28 neurotic patients in which dixyrazine was compared with "librium" (chlordiazepoxide) the preference of both the patients and the physicians was significantly in favour of dixyrazine. J. S. Bearcroft

729. Clinical Results with a New Phenothiazine Derivative: Dixyrazine (3412 U.C.B. or Esucos). (Résultats cliniques d'un nouveau dérivé phénothiazinique: la dixyrazine (3412 U.C.B. ou esucos))

A. Benruel. Acta neurologica et psychiatrica Belgica [Acta neurol. belg.] 61, 697-705, Aug. [received Oct.], 1961. 18 refs.

The results of the treatment of 50 male patients with "dixyrazine" ("esucos") are described in this paper from the Centre Neuropsychiatrique Militaire, Antwerp. The drug is a phenothiazine derivative, but in addition contains a piperazine nucleus which is found in other recent drugs and which is thought to produce the antipsychotic effects and the Parkinsonian side-effects. It has also a methyl radical on the second carbon in the lateral chain, which is believed to have antidepressive and anti-anxiety effects. The usual dosage of the drug was 25 to 150 mg. per day.

Of the 50 patients, whose ages ranged from 17 to 53 years and whose various psychiatric illnesses were of many diagnostic categories, 18 responded well, 23 improved, and 9 showed no improvement. The action of the drug on the psychotic process in schizophrenia was poor. On the other hand its tranquillizing effects upon. states of agitation and aggression were impressive. Its most useful role seemed to be in the treatment of acute neurotic conditions with or without anxiety, excitability, instability, and aggression. Patients with certain kinds of depression seemed also to be remarkably helped. Side-effects were few and occurred only with larger doses. Slight tachycardia was infrequent. Somn'olence occurred in 11 patients, while other effects included lacrimation, excess salivation and perspiration, and seborrhoea. In 7 patients extrapyramidal symptoms developed, these including "cogwheel" rigidity, hyperkinesis, torsion spasm, difficulty in speaking and eating, and drooling. The symptoms disappeared when the drug was discontinued. One illustrative case history is presented in J. S. Bearcroft detail.

Paediatrics

730. Maternal Health in Early Pregnancy and Congenital Defect. Final Report on a Prospective Inquiry A. D. McDonald. British Journal of Preventive and Social Medicine [Brit. J. prev. soc. Med.] 15, 154-166, Oct., 1961. 5 refs.

The author of this paper from Guy's Hospital Medical School, London, describes a prospective survey of 3,295 women who were interviewed early in pregnancy. The total number of children born alive to these patients was 3.116: there were 63 stillbirths. In 1959, when the children were 3 to 6 years old, 2,906 (95%) were traced and examined for abnormalities. It was found that the number of children with major malformations of the central nervous system was 21 (an incidence of 6.6 per 1,000 births), with mongolism 6 (1.9 per 1,000), with severe mental defect not due to mongolism 11 (3.5 per 1,000), cerebral palsy 8 (2.5 per 1,000), congenital heart disease 15 (4.7 per 1,000) (2 of whom also had mongolism), cleft lip or palate 6 (1.9 per 1,000), pyloric stenosis 19 (6.0 per 1,000), congenital dislocation of the hip 3 (0.9 per 1,000), severe talipes 3 (0.9 per 1,000), hypospadias 5 (1.6 per 1,000), and inguinal hernia 35 (12.3 per 1,000). The total incidence of serious malformations was 28 per 1,000 births. In addition, asthma or eczema developed in 26 per 1,000 children and fits in 19 per 1,000.

A number of maternal factors in pregnancy were related to the incidence of malformations, including age, parity, employment, and attempted abortion, and illness, injury, or severe emotional shock in the first 12 weeks of pregnancy. Suggestive associations were found between heavy work and serious malformation (4 children in 28), febrile illness and serious malformation (8 in 148) and eye defect (10 in 148), pulmonary tuberculosis and malformation (6 in 61), and anaesthetics and eye defects (5 in 54).

C. O. Carter

NEONATAL DISORDERS

731. Erythroblastosis Fetalis Due to c Iso-immunization in Rh-positive Women

R. C. BORONOW. Obstetrics and Gynecology [Obstet. and Gynec.] 18, 574-578, Nov., 1961. 12 refs.

Erythroblastosis foetalis in babies born to Rh-positive women is rarely due to c isoimmunization, but when this does occur the disease may be severe and demand prompt treatment. Three such cases, in all of which one or more exchange transfusions were required, are described in detail in this paper from the Northwestern University Medical School, Chicago. The author estimates that 19% of the Caucasian population is Rh-positive and homozygous C, while less than 0.01% is Rh-negative and homozygous C; hence c iso-immunization is extremely unlikely in Rh-negative women. In Rh-positive mothers the diagnosis may be delayed unless

its possibility is borne in mind. Antenatal prediction may be achieved by performance of the direct and indirect Coombs tests and by genotype studies of both parents, particularly if there is a history of unexplained anaemia, jaundice, stillbirth, or neonatal death in previous infant,

732. Antenatal Diagnosis of the Rh Erythroblastotic Fetus

W. C. RIGSBY, N. VORYS, W. E. COPELAND, and J. C. ULLERY. Obstetrics and Gynecology [Obstet. and Gynec.] 18, 579-590, Nov., 1961. 29 refs.

There is no concise way to evaluate or predict the infant or fetus with erythroblastosis. A method for furthering the understanding of the disease has been offered. A crutch for antenatal prognosis with reference to Rh hemolysis has been discussed. This balance-sheet type of aid is open to revision or rejection when a more accurate method of prediction is available.

Systematic application of data and thought on the subject provide our only valid approach to this problem at present.—[Authors' summary.]

733. Heterospecific Pregnancy and ABO Incompatibility in the Newborn. (Гетероспецифическая беременность и ABO-несовместимость у новорожденных) К. G. Sokolova. Вопросы Охраны Материнства и Детства [Vop. Ohrany Materin. Dets.] 6, 67–72, Oct., 1961. 14 refs.

In the course of an investigation of blood incompatibility between mothers and their babies it was found that of 200 healthy full-time infants 26 had Rh incompatibility and 44 had ABO incompatibility. The incidence of jaundice was somewhat higher (86.3%) in the heterospecific group than in the homospecific cases (64.7%). The mean difference in the blood picture in regard to erythroblasts, reticulocytes, haemoglobin concentration, and erythrocytes in the two groups was within the normal limits of error. Of a second group of 15 children with symptoms of erythroblastic jaundice 3 were shown to have Rh incompatibility and 12 to have a different ABO grouping from that of the mother, although mother and child were both Rh-positive; the mothers were all of Group O, while 7 of the infants were of Group A and 5 of Group B. The blood of all the mothers showed a high titre of isoagglutination to the child's blood group when tested in salt and protein media (particularly in the latter). One child with blood of Group A died, and in this case only was the blood positive to the direct Coombs test.

The author concludes that "heterospecific pregnancy" may have little or no ill effects in the majority of cases, and that heterospecificity to one of the ABO factors is more common than Rh incompatibility. She stresses, however, that in spite of this, all cases of early infantile

jaundice should receive detailed clinical examination and serological investigation from the earliest possible moment so that the necessary measures may be taken.

[Nothing is said about the number of the mothers' previous pregnancies, if any, in this series. The practice of determining the blood group of both the parents early in pregnancy does not appear to prevail in the U.S.S.R.]

L. Firman-Edwards

734. Neonatal Oedema Due to Exudative Enteropathy D. G. COTTOM, D. R. LONDON, and B. D. R. WILSON. Lancet [Lancet] 2, 1009-1012, Nov. 4, 1961. 2 figs., 24 refs.

The authors of this paper from St. Thomas's Hospital. London, describe 2 infants (sisters) who were oedematous soon after birth and were found to have hypoproteinaemia without renal or hepatic disease. The first infant, who was admitted to hospital aged 2 weeks, died after 6 weeks, no special investigations to ascertain the possible cause of the disturbance of protein metabolism having been carried out. The second infant was subjected to full investigation. After intravenous injection of polyvidone there was increased excretion of the drug in the. faeces; in the xylose test only 11% of the administered dose was excreted (normal 22 to 32%). The widespread mucosal thickening of the small bowel observed in the radiographs after administration of barium suggested an exudative enteropathy from jejunal disease. There was no response to a rigid protein-free diet, casein hydrolysate, steroids, or salt-poor albumin given intraperitoneally. At the age of 7 months the infant was taking a glutenfree mixed diet well, but remained oedematous and the hypoproteinaemia was unchanged. The authors consider that the normal erythrocyte sedimentation rate and serum cholesterol level and the low serum globulin value indicated a hypercatabolic hypoalbuminaemia with protein exudation into the small intestine.

David Morris .

735. Intestinal Obstruction in the Newborn Infant R. E. LARSON, L. E. HARRIS, and H. B. LYNN. *Proceedings of the Staff Meeting of the Mayo Clinic [Proc. Mayo Clin.*] 36, 516–524, Sept. 27 [received Nov.], 1961. 20 refs.

During the 10-year period 1950-59 a total of 68 infants with intestinal obstruction were admitted to the Mayo Clinic. In 28 the obstruction was due to malformations of the anus and rectum (Type-3 lesions in 26). Colostomy was performed in 10 cases in this group with 5 deaths, primary abdominoperineal repairs in 13 cases with 4 deaths, and perineal anoplasty in 5 without mortality. In 4 of the patients subjected to abdominoperineal repairs suprapubic cytostomy was also performed. The over-all mortality in this group was 32%. Intestinal atresia and stenosis accounted for 16 cases in the series with 5 deaths (mortality 31%). Duodenal stenosis was present in one case and duodenal atresia in 6 cases; in the remainder there was atresia in the small intestine. Associated colonic or rectal stricture was observed in 2 cases and in several the lesions were multiple. Treatment consisted in either duodenojejunostomy or entercenteric or entercoolic anastomosis.

In 9 of the 68 cases there was incomplete rotation with Ladd's bands (mortality of 66%), midgut volvulus being present in 4 of them. Treatment was by rectification of the volvulus and Ladd's operation. Meconium ileus accounted for 5 cases (4 deaths), which were treated by exteriorization resection (2), resection and primary anastomosis (2), and removal of meconium (one case). Aganglionic (Hirschsprung's) disease was the cause of the obstruction in 4 patients, all of whom died between the 3rd and 20th days after colostomy. Miscellaneous lesions including idiopathic perforation of the ileum, duplication of the terminal ileum, and omphalocele accounted for the remaining cases.

The importance of early diagnosis and of full ancillary investigations, especially radiology, is emphasized. There was the usual high incidence of associated congenital anomalies (41%)—notably mongolism and prematurity. Since postoperative aspiration of the gastrointestinal contents is the commonest single factor responsible for hospital mortality routine gastrostomy is strongly advocated.

Andrew M. Desmond

736. Failure of the Heart after Undue Asphyxia at Birth E. D. Burnard and L. S. James. *Pediatrics* [*Pediatrics*] 28, 545-565, Oct., 1961. 18 figs., 34 refs.

This paper from the College of Physicians and Surgeons, Columbia University, New York, reports a study of 33 infants who showed signs of heart failure after suffering severe asphyxia at birth. Of these patients, all mature infants of normal mothers and none having erythroblastosis or congenital malformation, 19 died and the findings in this group are compared with those in the 14 survivors.

On x-ray examination the increased transverse diameter of the heart was the same in those who recovered as in those who died, though the survivors showed a considerable reduction in this diameter with time. Biochemical studies were carried out on blood from the umbilical artery, oxygen saturation, CO2 content, and pH being determined, while pCO₂ and buffer base were estimated by means of the Singer and Hastings nomogram. In the infants with an abnormal degree of birth asphyxia there was an initial acidosis greater than is normally found and the slower return to normal could be correlated with the clinical condition; the pH remained low except in those whose illness was brief. A profound metabolic acidosis with a considerable reduction in buffer base was found most frequently in thosewho died, but not exclusively so; the pCO2 varied widely, while oxygen saturation was reduced, demonstrating pulmonary insufficiency as evidenced by the hypoxia present in left atrial blood in 3 of the infants. Venous pressures were found to be considerably above normal in the ill babies. Whereas in 6 of the infants who died the radiographs were normal when first taken, 2 of these patients later developed changes suggestive of aspiration pneumonia, while in 2 others there was a bronchopneumonia-like appearance on the first film, in 3 a hyaline-membrane-like appearance, and in 3 focal atelectases. Although these appearances might seem to suggest different disease entities, the authors contend

that vascular congestion and the presence of transudate might well be the explanation. At necropsy the hearts of infants who died were anatomically normal, but with wide patency of the ductus arteriosus. The lungs showed congestion, oedema and haemorrhage, albuminous fluid in the alvoli, and in some cases hyaline membrane. Polymorphonuclear leucocytes were present in the pulmonary tissues in all but 3 of the cases, presenting an appearance varying from a sparse infiltration to a frank pneumonia in 3 cases.

Discussing these findings the authors emphasize that a single diagnosis was rarely possible and that clinically most of the babies were thought initially to have atelectasis from an obstructed airway at birth, combined in different cases with pneumonia, septicaemia, or brain damage, and this clinical speculation is supported by the post-mortem findings. All the infants who lived long enough showed striking clinical similarities, pointing to a patho-physiological disorder common to them all, which could be the attempt at compensation by the heart. while the variable clinical picture might have been due to the rate of failure of the right heart. Although the cause of the heart failure remains an enigma, it is clearly related to the metabolic disorder resulting from the undue degree of asphyxia at birth. David Morris

737. "Early" versus "Late" Feeding of Infants of Diabetic Mothers

J. P. Hubbell Jr., J. E. Drorbaugh, A. J. Rudolph, P. A. M. Auld, R. B. Cherry, and C. A. Smith. New England Journal of Medicine [New Engl. J. Med.] 265, 835-837, Oct. 26, 1961. 10 refs.

Infants of diabetic mothers under the care of the Joslin Clinic, Boston, were studied at the Boston Lying-in Hospital to test the effect of early feeding on mortality from hyaline membrane disease. The mother was delivered not later than the 37th week. Caesarian section was performed if labour could not be easily induced or the condition of the foetus was questionable. A total of 96 infants were divided at random into 2 equal groups which were placed on early and late feeding regimens respectively. The early feeding programme aimed at giving 0.45% sodium chloride in 5% glucose and water in amounts of 30 ml. per lb. (66 ml. per kg.) body weight per 24 hours, feeds being given by gastric lavage or bottle every 4 hours or, if necessary, by injection into the umbilical vein. The average age at the first feeding in this early-fed group was 4 hours (range 1½ to 7 hours). At 48 hours of age these infants were placed on the routine hospital feeding schedule. The late-fed group received nothing for 48 hours and then started on the routine hospital feeding schedule.

All the infants were carefully observed for respiratory distress. When necessary a chest radiograph was taken to exclude other disease and to detect generalized reticulogranularity. Treatment with antibiotics and oxygen was given if a diagnosis of "idiopathic respiratory-distress syndrome" was made. Six deaths associated with hyaline membrane formation occurred, 5 among the early-fed and one among the late-fed infants. This difference was considered not to be statistically significant

because of the small numbers. Morbidity, largely in the form of idiopathic respiratory distress, which was assumed to signify hyaline membrane formation, was about equally distributed in the 2 groups. Weight loss was significantly less with early feeding at both 48 and 72 hours. The serum bilirubin level was also lower in the early-fed than in the late-fed infants, significantly so at 72 hours, and fewer of the early-fed infants had peak concentrations of unconjugated serum bilirubin above 20 mg. per 100 ml.

Aspiration was found not to be a real risk in the feeding of very young infants in this series. The authors suggest that a larger series of cases will be needed to prove the effect of early feeding in the treatment of hyaline membrane disease, but the reduction of the serum bilirubin level in the early-fed group indicates a definite metabolic advantage of early feeding in a group notoriously prone to hyperbilirubinaemia. Haemodilution was considered not to be the cause of the reduction of bilirubinaemia since this was most evident at 72 hours, when fluid had been given to both groups. Moreover, the average haematocrit reading in the early-fed group was not significantly lower at 48 hours than in the late-fed group. Ferdinand Fok

CLINICAL PAEDIATRICS

738. Evaluation of an Enlarged Cardiothymic Image in Infancy. Thymolytic Effect of Steroid Administration S. P. Griffiths, O. R. Levine, D. H. Baker, and S. Blumenthal. American Journal of Cardiology [Amer. J. Cardiol.] 8, 311-318, Sept., 1961. 5 figs., 23 refs.

The authors, writing from the Babies Hospital (Columbia University), New York, discuss the difficulties encountered in the assessment of the cardiac outline in mediastinal radiographs of infants with an enlarged thymus gland. In this study they made use of the thymolytic effect of steroid drugs to shrink the thymus in the examination of some 20 infants, of whom 5 who presented a particularly difficult diagnostic problem are described in detail. The various steroids employed were given in a dosage equivalent to 5 mg. of cortisone per kg. body weight. Accompanying radiographs demonstrate that maximum shrinkage of the thymus occurred in 5 to 7 days, and regrowth of the gland in a further 2 weeks.

The first infant, who was seen at the age of 3 months before undergoing herniorrhaphy because of the finding of a cardiac murmur, had bradycardia (pulse rate 68 per minute) and electrocardiography (ECG) revealed complete atrio-ventricular block and inversion of T waves in Leads I, aVL, V5, and V6, though these waves were upright in Leads V1 and V2. The cardiac outline was obscured by a large mediastinal shadow, but after the administration of prednisone, which produced involution of the thymus, the heart was clearly shown to be dextroposed. Reversal of the ECG leads confirmed that the previous T-wave inversion was a manifestation of 13 months demonstrated corrected transposition and a left-to-right shunt which was most probably due to a

ventricular septal defect. The second infant was adopted at the age of one month but at age 4 months was found to have a cardiac murmur and apparent gross cardiomegaly in the radiographs, whereupon the possibility of legally abandoning the adoption was raised. However, the administration of steroid drugs demonstrated that the mediastinal shadow was due to an enlarged thymus gland, the cardiac outline being then quite normal and the murmur apparently functional.

In the third infant radiography revealed an enlarged cardiac and supracardiac shadow which did not alter with steroid therapy, and a final diagnosis of a persistent. left superior vena cava and coarctation of the aorta was demonstrated by angiocardiography. In the fourth infant, who was examined radiologically at the age of 3 days because of the finding of a cardiac murmur, the radiograph showed a wide mediastinal shadow and even at the age of 2½ years this was still present, the straight upper left cardiac border suggesting the diagnosis of corrected transposition. Steroid therapy resolved this shadow, and a final diagnosis of the tetralogy of Fallot. was confirmed by angiography. The fifth case is recorded to demonstrate the spontaneous resolution of an enlarged mediastinal shadow between the ages of 2 and 10 months in an infant with congenital heart disease. H. G. Farquhar

739. Hyperplasia of the Adrenal Medulla in Hypertension of Children

D. BIALESTOCK. Archives of Disease in Childhood-[Arch. Dis. Childh.] 36, 465-473, Oct., 1961. 11 figs., 35 refs.

Though hypertension in childhood is rare, 20 children with a persistently raised blood pressure but without nephritis or cardiovascular disease have been seen at the Royal Children's Hospital, Melbourne, over the 7-year period 1952-9. The author describes the clinical features in 3 of these children, who all died, together with the histological changes found in the adrenal glands and kidneys in the 2 on whom necropsy was performed. The first 2 patients, boys aged 5 and 11 years respectively, were found to have marked hypertension (260/175 mm. Hg) and at necropsy, apart from the grossly enlarged heart, no obvious abnormality was present. Histological examination of the adrenal glands from both patients showed that the cortex was normal, but that the medulla consisted of large numbers of hypertrophic, vacuolated, cosinophilic cells with pale, oval, eccentrically placed nuclei. Pressor substances were not isolated from these cells. The third patient was a girl aged 12 years with similar clinical features, but in this case necropsy was not performed and no histological specimens were obtained. Histological examination of the kidney in the first patient (the boy aged 5) showed that the cells of the juxtaglomerular apparatus of Goormaghtigh and also of neighbouring hypertrophic renal tubules were filled with dense basophilic granules, and the author suggests that these granules may be the source of a renal pressor substance. He concludes, however, that local renal factors are unlikely to have been the only cause of the hypertension, and cites hyperplasia of the adrenal medullary cells, which was marked in 2 of the 3 R. M. Todd cases, as a likely primary cause.

740. Effectiveness of Adenovirus Vaccine in Children with Repeated Acute Respiratory Illnesses

P. J. KOZINN, H. WIENER, and J. J. BURCHALL. *Journal of Pediatrics* [J. Pediat.] 59, 669-673, Nov., 1961. 25 refs.

At Maimonides Hospital, Brooklyn, New York, 104 children with a history of recurrent respiratory illnesses were each given two injections of a hexavalent adenovirus vaccine. No untoward reactions were noted. The vaccine failed to produce any significant antibody response in a large proportion of the children. Further no constant relationship was noted between clinical improvement and a rise in virus neutralizing antibody titre.

It is concluded that "unless and until a large-scale controlled study shows statistically significant increases in antibody titre and decreases in respiratory illnesses attributable to the use of the vaccine, there is not sufficient evidence to justify its routine use in paediatrics".

John Fry

741. **Pseudoparesis.** (Pseudoparesen) H. Spiess. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **109**, 438–441, Oct., 1961. 6 refs.

The author discusses psychogenic pseudoparesis with reference to the case histories of 9 children admitted to the Paediatric Clinic of the University of Göttingen. He asserts that a diagnosis of psychogenic pseudoparesis must never be made until a careful examination has excluded all somatic causes of paralysis, whether traumatic, inflammatory, or toxic, and metabolic disturbances of joints, bones, and muscles. Normal neurological findings give strong support to a diagnosis of pseudoparesis. It must be borne in mind, however, that paresis may be. simulated by pain, as occurs in subluxation of a joint or in acute rheumatism; that the reflexes may be normal at the onset of an organic lesion which later gives rise to paralysis; and that weak or absent tendon reflexes may be present in such conditions as periodic paralysis—the metabolic disorder in which the blood potassium level is lowered—and in adynamia episodica hereditaria, in which the blood potassium level is raised. The presence of spastic paralysis on walking but of abasia-astasia when the patient is in bed is suggestive of an hysterical origin of the paresis.

Careful history-taking may be of the greatest help in establishing the diagnosis. A history of onset of the paresis occurring in a child during a period of anxiety concerning work at school sometimes conveys the direct impression that the child's physical condition is a picture of his mental attitude of rejection of a specific situation. Any attempt to overcome this attitude is successful only if an indirect approach is made through suggestion. while talking to the child or in the therapy employed. The author has found that an unstable neuropathic constitution generally underlay the neurotic reactions of his patients to psychical stresses. Such constitutional defects were observed years after the paresis had disappeared completely. He believes that in children the prognosis of this condition is good, provided that the hysterical component is recognized and both symptoms and the exogenous circumstances leading up to them are treated early and intelligently. E. S. Wyder

Public Health and Industrial Medicine

742. The Effects of Anaesthesia and Elective Surgery on Old People

B. R. SIMPSON, M. WILLIAMS, J. F. SCOTT, and A. C. SMITH. *Lancet* [*Lancet*] 2, 887-893, Oct. 21, 1961. 2 figs., 27 refs.

In view of reports of dementia after anaesthesia and surgery in old people it was decided to review the state of social integration of all patients over 65 before and after admission for elective surgery to the Oxford United Hospitals in 1959. One author visited the 741 patients in their homes before and 3 months after admission to assess physical and mental capability, personality, and social integration: 6 functions were thus scored in 5 grades. More elaborate mental testing was performed on 250 patients selected from the group before and after operation, 32 variables being analysed by multiple regression equations on a computer. Analysis was made separately to determine the relative effect, if any, of general or local anaesthesia (including spinal and extradural methods).

In statistical terms anaesthesia itself had no effect on physical or mental capability, personality, or social integration of the patients studied. A control group of 61 from whom anaesthesia and surgery had to be withheld showed a general tendency to deteriorate, but those who underwent surgery showed a general improvement in social-integration scores. When operation relieved symptoms many patients lived fuller lives; provided symptoms were relieved, the severity of operation was immaterial to the outcome. Of the 223 (33%) who were "improved" or "much improved" after elective surgery, the improvement was attributable directly to surgery in 205. Of the 89 (12%) who deteriorated after surgery, a number did so for reasons unconnected with the disease for which surgery was undertaken, and the rest because of an increase in the severity of the disease, often a malignant one. The death rate, excluding cases treated conservatively, was 8%, but surgery or its immediate chest complications accounted for only 2.2% of deaths.

The authors discuss recent improvements in anaesthesia and general care of old people which have contributed to their results, and conclude that there is no justification for denying surgery to old people because of anaesthetic risks, though the margin for surgical and anaesthetic error is smaller.

J. N. Agate

743. Air Pollutants and Incidence of Respiratory Disease F. C. DOHAN. Archives of Environmental Health [Arch. environm. Hlth] 3, 387-395, Oct., 1961. 1 fig., 12 refs.

Sickness absences lasting more than 7 days among women factory workers in 8 towns in the U.S.A. were compared in relation to air-pollution measurements in those towns, in particular, measurements of suspended particulate sulphates. For only 5 of the towns were

measurements of sulphates available, but in these towns respiratory illness rates were highly correlated with the mean sulphate pollution of the atmosphere.

[The methods of sampling the air and estimating the pollutants, the sampling sites, and the time of the year when samples were taken are not given, and the number of estimations made in the 3-year period—21 to 25 in 4 of the cities—seems very small. It is therefore difficult because of the paucity of the data published to assess the significance of the findings.]

J. Pemberton

EPIDEMIOLOGY AND IMMUNIZATION

744. An Epidemic of Benign Lymphocytic Meaingitis in Cardiff, 1960

A. Guy. Medical Officer [Med. Offr] 106, 245-247, Oct. 20, 1961. 2 figs.

The number of cases of benign lymphocytic meningitis admitted to the infectious diseases hospital in Cardiff showed a sharp rise from 17 in 1958 to 41 in 1959 and 129 in 1960, and it is known that a number of milder cases were treated at home; the hospital admissions were highest in July and August, 1960 (36 and 37 respectively), and the illnesses ranged from the mildest symptoms to overt meningitis. Of 149 cases in the city (93 in males and 56 in females), 103 were in children under 15; among the 129 hospital cases there were 86 patients under 15 (66.7%), and the sex ratio of males to females under 15 was 1:0.49, and 15 and over 1:0.91. The author notes the similarity of sex and age ratios to those in cases of non-paralytic poliomyelitis notified in England and Wales in 1958—namely, patients under 15 years 73.7%; males to females under 15 years of age 1:0.45, 15 and over 1:0.93. Of the 35 virus-positive cases admitted to hospital, E.C.H.O. 9 virus was found in 28 cases and Coxsackie B5 virus in 7. No evidence was found of a focus of infection in any area or in one particular type of housing. F. T. H. Wood

745. The Use of Vaccinia Hyperimmune Gamma-globulin in the Prophylaxis of Smallpox

C. H. KEMPB, C. BOWLES, G. MEIKLEJOHN, T. O. BERGE, L. ST. VINCENT, B. V. S. BABU, S. GOVINDARAJAN, N. R. RATNAKANNAN, A. W. DOWNIE, and V. R. MURTHY. Búlletin of the World Health Organization [Bull. Wld Hlth Org.] 25, 41–48, 1961.

For the purposes of this cooperative study of the use of vaccinia hyperimmune γ globulin (V.I.G.G.) in the prophylaxis of smallpox, index cases were collected from among admissions to the Infectious Diseases Hospital, Tondiarpet, Madras. In each case selected the patient came from a family in which there had been no previous case of smallpox within the past month, the occurrence of the index case being the reason for the revaccination of

family contacts. The definition of family contact was based on the following criteria: (1) intimate room contact; (2) individuals joining the family after the index case was admitted to the hospital, but exposed upon visiting the hospital frequently; and (3) no proved history of clinical smallpox in the past; persons were not excluded who reported having smallpox in the past but showed no visible scars. The contacts of 97 index cases. selected at random, received V.I.G.G. and were also vaccinated, whereas the contacts of 111 index cases were vaccinated only and constituted the control group. The dosage of V.I.G.G. was 5 ml. for children under 5 years and 10 ml. for adults, given intramuscularly. Swedish, British, and United States products were used and were essentially of equal potency. All the products had been obtained from the plasma of recently vaccinated young adult donors and contained 12% of V.I.G.G.

Among 326 contacts receiving V.I.G.G. during the follow-up period 5 cases of smallpox were identified. Among 379 controls there were 21 cases of smallpox. There were 3 individuals in the V.I.G.G. group and one control subject who contracted smallpox a considerable time after known exposure, presumably from a source other than the index case. In none of these 4 cases had successful revaccination been carried out and in the absence of successful revaccination the protection passively given by V.I.G.G. had probably disappeared after 2 to 3 weeks, leaving the patient again susceptible to the disease. Of 7 newborn infants exposed to smallpox infection in utero, at birth, or soon afterwards, all of whom received 5 ml. of V.I.G.G., 3 developed mild clinical smallpox. All 3 died, but the expected death rate in newborn infants infected in utero or at birth by their own mothers is exceedingly high and the appearance of clinical smallpox in only 3 of the infants is probably of significance. As the supply of V.I.G.G. is limited it is likely that its use will be restricted to those especially at risk, such as unvaccinated family contacts, the newborn, and pregnant women. R. G. Mever

746. TAB Vaccines—an Assessment of their Value as Prophylactics against Enteric Fever

J. H. JACKSON. South African Journal of Laboratory and Clinical Medicine [S. Afr. J. Lab. clin. Med.] 7, 93-107, Sept. [received Nov.], 1961. 39 refs.

Assailed by doubts as to the efficacy of T.A.B. endotoxoid in preventing typhoid fever; the author, writing from the State Health Department, Durban, Natal, reviews his experience in institutions in Natal and Zululand. One example is quoted of 12 out of 14 properly immunized persons developing typhoid fever and another instance reported in which hygienic and sanitary measures alone prevented the disease developing in 1,659 unimmunized persons exposed to infection.

Serological investigation of new arrivals at the institutions (representative of the general non-European adult population) showed that the vaccine was not effective in stimulating a rise in agglutinin titre and that the laboratory Widal and Vi tests were variable. However, it was concluded that (1) a Salmonella typhi O agglutinin titre above 1:640 was likely to be diagnostic

of typhoid fever whether or not the subject had been immunized, while if he had not been immunized within the past 4 weeks a titre of 1:320 was diagnostic; (2) in an unimmunized person a titre of 1:160 was suggestive of typhoid fever, but was not diagnostic unless the titre was rising; and (3) H agglutinins had little diagnostic value and that in paratyphoid-B Widal titres also had little diagnostic value.

Discussing the nature of immunity to typhoid fever, the author suggests that relationship of antibodies to immunity is a possible reason for the inefficiency of T.A.B. endotoxoid. An analogy is drawn with premunity dependent on the stimulus of the living organism being present in the body, and a living avirulent vaccine or a dead vaccine incorporating some "vital" substance is suggested as being necessary for satisfactory immunization. The use of the present vaccine is considered to be indicated in persons who are going into endemic areas, in key personnel, in disaster conditions in which there is a general breakdown of preventive services, as in the case of floods, droughts, or earthquakes, and possibly in the case of residents in the home of permanent carriers of typhoid organisms. The contraindications are many for example, in an incubating case of typhoid fever and in established epidemics—and it is considered that the immunity produced by the vaccine is no better than immunity due to endemic infection. The author emphasizes that reliance should be placed on dealing with paths of transmission of infection rather than on immunization.

[This is a thought-provoking article, especially as it illustrates once again that antibody titres are only an index to, and not a guarantee of, immunity.]

Kurt Schwarz

747. Illness after Whooping Cough Vaccination, J. M. H. HOPPER. *Medical Officer* [Med. Offr] 106, 241-244, Oct. 20, 1961. 18 refs.

In a period of 18 months 1,700 infants in Northumberland received 3 injections of pertussis vaccine without reported ill effects, and 40 others suffered upset or illness —an incidence of 23 per 1,000; in addition, 12 infants vaccinated with combined diphtheria, tetanus, and pertussis vaccine were also affected (found to be the same incidence). The illness ranged from irritation at the site of injection through various degrees of generalized irritation to one of a state of collapse. Comparison with a random sample of 52 non-affected infants showed that a family history of eczema, asthma, hay-fever, and allergic skirt rashes was twice as common in the affected group, and of fits 4 times as common; further, infections of the respiratory and the gastro-intestinal tracts were more frequent in the latter group. The author notes that no environmental factor was involved, and considers that the cause appears to be twofold—the pertussis antigen and the individual constitutional element.

F. T. H. Wood

748. Current Status of Immunization. [Review Article] M. Brown. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 765-769, Sept. 30, 1961. 18 refs.

INDUSTRIAL MEDICINE

749. The Action of Artificial Dust Mixtures (Containing Rare Metals and Silica) on the Body. (Действие на организм искусственных пылевых смесей (соединения редких металлов и двускись кремния) О. Ја. Моспечскаја. Гизиена и Санитария [Gig. j Sanit.] 26, 18–24, Sept., 1961. 4 figs., 5 refs.

The author has investigated in rats the effect of intratracheal injections of mixtures of 2.5 mg. of silicon oxide plus 47.5 mg. of the oxides of various rare metals suspended in sterile physiological saline, each injection consisting of 50 mg. of dust in 0.7 ml. of saline; in all cases 90% of the dust particles were less than $2\,\mu$ in diameter. The rare metals used in the mixtures were molybdenum, zirconium, titanium, and tungsten. After either 4 or 8 months the animals were killed and the lungs examined macroscopically and histologically; a small group of 5 control animals received no dust.

It was found that the dust mixtures containing small amounts of silica differed in their action on the lungs both from that of the oxides of the rare metals alone and from silica alone given in the same doses. The amount of silica being equal, the character of the action of the dust mixture depended on the nature of the metallic oxide. The addition of silica was shown to enhance the specific action of each of the metallic oxides used. In some cases the silica modified the lesion produced by the metallic oxide—thus, for example, when mixed with zirconium oxide signs of metaplasia were found in the lung tissue. In view of the fact that the fibrogenic action of silica differs essentially from that of other forms of fibrosis of connective tissue in the lungs, the author suggests that in these experiments with inhalation of mixed dusts the final effect is not one of simple summation, but of a definite combination of the mechanisms of the pathogenic action of the two constituent dusts. Basil Haigh

750. Ascorbic Acid Metabolism in Experimental Silicosis. (К вопросу об обмене аскорбиновой кислоты при экспериментальном силикозе)

Z. Ja. Dolgova. Гивиена Труда и Профессиональные

Заболевания [Gig. Truda prof. Zabolev.] 5, 24—27, Aug., 1961. 8 refs.

The author has investigated the distribution of ascorbic acid in the organs of guinea-pigs and white rats in which experimental silicosis had been induced by the intratracheal insufflation of quartz dust (containing 98% free silica, the dosage being 50 mg. per rat and 100 mg. per guinea-pig) in 1 ml. of physiological saline solution). The development of silicosis was confirmed by histological examination of the lungs of the experimental animals; the ascorbic acid was given at different dose levels to both the experimental and control animals.

The tests showed that in experimental silicosis ascorbic acid synthesis in the rats was increased, whereas in guineapigs its concentration in the liver, kidneys, and adrenal glands was decreased, especially in animals receiving the minimum daily dose of vitamin C; the concentration of the vitamin in the guinea-pigs' lungs fell irrespective of the dose of vitamin given. One month after administra-

tion of dust to the rats their ascorbic acid synthesis was increased, but 3 months after exposure the rate of synthesis was reduced. It was noted that only 24 hours after injection of quartz dust the ascorbic acid synthesis in the lungs of the rats was increased, and the concentration of the vitamin in certain organs of the guinea-pigs was lowered. This finding suggests a neuro-humoral mechanism of disturbance of the ascorbic acid metabolism in response to experimental silicosis. The author concludes that in view of the increased ascorbic acid consumption in silicosis, administration of vitamin C is indicated in the treatment of this disease.

Basil Haigh

751. The Action of Silicate Bacteria on the Development of Silicosis in the Lungs. (Экспериментальное ивучение влияния силикатных бактерий на развитие силикотического процесса в легких)

R. K. Mel'ničenko. Гивиена Труда и Профессиональные Заболевания [Gig. Truda prof. Zabolev.] 5, 27—

30, Aug., 1961. 6 refs.

Silicate bacteria, isolated from the soil or elsewhere, decompose alumosilicates. Their use has therefore been suggested for the elimination of silica-containing dust from the body, and hence for the prevention and treatment of silicosis. In the present studies silicate bacteria isolated from the lungs of jays were used in three series of experiments, as follows: (1) 11 white rats received an intratracheal injection of 50 or 25 mg. of silica dust plus 0.5 ml, of a suspension of silicate bacteria in physiological saline, the bacterial injection being repeated monthly; (2) 20 rats received 50 or 25 mg. of silica dust but no bacteria (controls); and (3) 21 rats received 50 mg. of silica suspended in 1 ml. of physiological saline, followed after an interval of one month by injections of silicate bacteria at monthly intervals, the aim of this experiment being to study the effect of the bacteria on formed silicotic lesions. The injections were given into the trachea under ether anaesthesia and 1 ml. of suspension contained 109 bacterial cells. In all the animals the respiratory quotient and the total collagen content of the lungs were determined and histological and nakedeye examination of the changes in the lung tissues was carried out.

The author concludes from the results of these experiments that the strain of silicate bacteria used did not inhibit the development of silicosis.

Basil Haigh

752. The Treatment of Silicosis and Its Complications. (Современное состояние вопроса о лечении силикоза и его осложнений)

N. A. Senkevič. Гигиена Труда и Профессиональные Заболевания [Gig. Truda prof. Zabolev.] 5, 52— 57, Sept., 1961. 34 refs.

In this comprehensive review of silicosis and its complications the author classifies treatment into (1) "aetiological", (2) pathogenetic, and (3) treatment of complications. Aetiological treatment includes measures designed to prevent the entry of silica into the body as well as measures to promote its excretion or to suppress its pathogenic action. Alkaline inhalations increase the

solubility of silica, and its action on the lung tissues may be modified by inhalation of aluminium powder, sodium calciumedetate, certain mineral waters, or electrically active aerosols. In pathogenetic treatment possible methods include (1) the action of biogenic stimulators (tissue therapy), (2) inhalation of procaine, (3) the administration of cortisone and ACTH (especially in rapidly progressive silicosis uncomplicated by tuberculosis), or of salicylates, or hyaluronidase, these 3 drugs being given for their anti-inflammatory action, (4) a diet rich in protein and vitamins, especially methionine, casein, and nicotinic acid, (5) spa therapy (in uncomplicated cases), (6) breathing exercises (in mild cases uncomplicated by emphysema), (7) irradiation of the chest with ultraviolet light to promote the pulmonary circulation and aid the excretion of silica, (8) the use of broncholytic drugs such as euphyllin or ephedrine given by aerosol inhalation or intravenously, and lastly (9) oxygen therapy, preceded by bronchial dilator drugs, in cases of severe respiratory failure.

In the treatment of the complications of silicosis the presence of bronchitis and bronchiectasis may require the use of antibiotics given as aerosols, expectorants, and the inhalation of enzymes (trypsin) to liquefy the bronchial secretions; in pneumonia antibiotics and anti-inflammatory drugs together with trypsin may be given; in silico-tuberculosis treatment includes general hygienic and dietary measures, antituberculous drugs (either alone or in conjunction with cortisone or tuberculin), and, in rare cases, collapse therapy or surgical resection. Prophylactic administration of PAS or isoniazid is advocated in those with a high occupational risk of silico-tuberculosis, for example, sand-blasters.

Basil Halgh

753. A Pilot Enquiry into Byssinosis in Two Cotton Mills in the United States

C. B. McKerrow and R. S. F. Schilling. Journal of the American Medical Association [J. Amer. med. Ass.] 177, 850-853, Sept. 23, 1961. 13 refs.

A review of the literature suggests that dust concentrations in cotton-mill cardrooms in the United States may be lower than those in English mills, in one of which nearly 40% of the cardroom workers were found to have symptoms of byssinosis. In England and Wales between 1942–4 and 1957–9 recorded deaths from byssinosis have risen from 14 to 122 and disability pension awards from 20 to 910.

Two mills were studied in the United States in 1960, both of which had spinning-counts comparable to those in English mills studied previously and showed a high prevalence of the disease. In one of the two mills (Mill 2) information was obtained by questionary from 17 cardroom workers and 18 other workers; their ventilatory capacity was also measured, it having been shown (Brit. J. industr. Med., 1958, 15, 75; Abstr. Wld Med., 1958, 24, 313) that exposure to cotton dust is associated with a diminished maximum breathing capacity during the course of a day's work. The dust sampling method, selection of workers for study, diagnostic criteria, and method of testing ventilatory capacity are described in detail.

In Mill 1 current health records showed there were 4 cardroom workers with a typical history of byssinosis; and dust samples taken near the carding machines were found to have lower concentrations of total dust than samples from English mills.' In Mill 2 one cardroom worker gave a typical history of byssinosis, and 2 others had chest symptoms which may have been related to exposure to cotton dust. Concentrations of dust showed a similar trend to those in Mill 1. It was found that chest symptoms were more frequent among cardroom's workers than others, and persistent cough was significantly more prevalent among them. Comparison between ventilatory capacity on a Monday morning and afternoon showed some decline in the afternoon in both groups of workers investigated, but the reduction was significantly greater in the cardroom workers than in the

It is suggested that, "if byssinosis proved to be a less serious problem in the United States than in England, it should be possible to find out how far this may be due to differences in dust concentrations, atmospheric pollution, and smoking habits".

L. W. Hale

754. Exposure to Parathion: Measurement by Blood Cholinesterase Level and Urinary p-Nitrophenol Excretion J. D. Arterberry, W. D. Durham, J. W. Elliott, and H. R. Wolfe. Archives of Environmental Health [Arch. environm. Hlth] 3, 476-485, Oct., 1961. 3 figs., 8 refs.

Of the 71 cases of illness due to parathion poisoning reported in the central area of the State of Washington in 1958 only 62 were occupational in origin, the remainder occurring in the children and wives of orchard workers who lived near the orchards. At the Communicable Disease Center, Wenatchee, Washington, an exposure study based on measurement of the blood cholinesterase level and the urinary p-nitrophenol excretion was made on 115 subjects divided into 7 groups according to their decreasing probable exposure.

The group with the highest potential exposure, namely, mixing plant personnel, was the only one showing a definite decrease in blood cholinesterase activity and this was limited to the erythrocytes, the plasma activity being within the normal range. The urinary excretion of p-nitrophenol was found to be a more sensitive indication of exposure. All 5 of the highest exposure groups excreted significant amounts even when the erythrocyte and plasma cholinesterase levels were within normal limits. This absence of correlation was not found in the cases of poisoning with parathion, classified according to their symptomatology, suggesting that almost any person who works with parathion is in danger of poisoning if he becomes careless. All these subjects excreted amounts of p-nitrophenol ranging from 0.57 to 32.2 p.p.m. for mild and moderate cases and from 1.6 to 11.6 p.p.m. for the severe and fatal cases. The fact that the highest value occurred in a case of moderate severity indicates that while the level of urinary p-nitrophenol excretion is a sensitive measure of exposure to parathion it is not a reliable measure of the severity of poisoning. The excretion of p-nitrophenol is rapid, disappearing from the urine about 48 hours after cessation of exposure,

in contrast to the blood cholinesterase activity, which remains depressed for about 30 days in the plasma and 80 to 100 days in the erythrocytes. A good response to atropine appeared to be the most reliable criterion of poisoning, only one out of 23 persons to whom it was given showing no response.

Ethel Browning

755. Possible Nephrotic Effect of Calcium Disodium Ethylenediamine Tetraacetate. (Zur Frage der nephrotoxischen Wirkung des Calciumdinatriumäthylendiamintetraacetats)

V. LACHNIT. Archiv für Gewerbepathologie und Gewerbehygiene [Arch. Gewerbepath. Gewerbehyg.] 18, 495-505, 1961. 37 refs.

The calcium disodium salt of ethylenediamine tetraacetate (sodium calciumedetate) is generally regarded as the best chelating agent for removing lead; it is free from the disadvantage of producing severe hypocalcaemia, but it has been stated to cause renal injury, in the form of toxic nephrosis, when given in overdosage or to susceptible individuals. Some proprietary preparations, however, contain very variable concentrations and their use may lead to severe overdosage. In a previous investigation of a large series of cases of lead poisoning (Wien. Z. inn. Med., 1959, 40, 321) the author found pathological urinary manifestations or an increase in residual nitrogen.

The present study, carried out at the Second University Medical Clinic, Vienna, included estimations of renal function (as shown by creatinine clearance), the phenolred test, and examination of urinary sediment. No significant deterioration in renal function was observed, and although the creatinine clearance rose in 13 cases and fell slightly in 6, in only one case was the level pathological. The phenol-red test results were within normal limits or nearly so except in 2 cases in which the urinary sediment contained abnormal elements before treatment. · Sodium calciumedetate was given by injection in the first stages, in a dosage of 0.12 g. in 150 to 200 ml. of 5% laevulose solution in physiological saline, this being increased to 2.4 g. if well tolerated. Later, slow intravenous infusion was substituted and a second course given after an interval of 7 days; it is claimed that this method avoids the loss of trace elements such as zinc. copper, and magnesium, and entails no risk of renal damage. The discredit thrown by earlier authorities on this chelating agent is ascribed to inexact information as to the composition of proprietary preparations which led to overdosage. Ethel Browning

756. Further Studies on the Toxicity of Some Tetra and Trialkyl Lead Compounds

J. E. CREMER and S. CALLAWAY. British Journal of Industrial Medicine [Brit. J. industr. Med.] 18, 277-282, Oct., 1961. 8 refs.

The likelihood that tetramethyl lead will soon be more widely used as an "anti-knock" additive to petrol has led to experimental studies of the toxicity of this and related substances. Trimethyl lead chloride in 0.9% saline solution was injected into the peritoneum of rats. Initial collapse and paresis of the hind legs disappeared after

40 minutes, but in fatal cases hyperexcitability and convulsions followed. The L.D.50 was estimated to be 25.5 mg. per kg. body weight. Tetramethyl lead was injected intravenously in an ethanol solution in rats and rabbits up to a maximum dose of 34 mg. per kg. body weight. Larger doses had to be given orally in arachis oil as the intravenous vehicle was too toxic. The signs of poisoning were similar to those described above, and the L.D.30 for tetramethyl lead was 109.3 mg. per kg. In rats the inhalation of tetramethyl lead vapour produced hyperexcitability and tremors exactly similar to those seen in rats poisoned with trimethyl lead chloride or tetraethýl lead, bút the dose required was very much higher than for these latter substances. Tremors and convulsions did not occur after giving propyl lead compounds. However, an intraperitoneal injection of 20 mg. of tripropyl lead chloride (dissolved in one part of dimethyl diformamide and two parts of arachis oil) per kg. body weight produced in rats an unsteady gait, weak hind legs, and a peculiar stiff posture with humped back and erect tail. The L.D.50 was about 26.67 mg. per kg. Rats given up to 40 mg, of tetrapropyl lead per kg. showed no signs of poisoning, but a high oral dose (395 mg. per kg. in arachis oil) produced signs comparable to. those caused by tripropyl lead.

The distribution of trimethyl and tripropyl lead in the tissues of the rats was then estimated. Trimethyl lead was found in high concentration in the blood and also appreciable quantities in the liver and kidney, whereas only traces of tripropyl lead appeared in the blood. However, when these compounds were added to whole blood in vitro 90% of each compound could be recovered from the erythrocytes. Tetraethyl lead has been shown to be converted rapidly to the triethyl form in the tissues. This conversion to the tri-form appears to occur much more slowly with the tetramethyl and tetrapropyl leads. The incubation of rat-brain slices in Krebs-Ringer phosphate medium with the various organic lead compounds showed that frimethyl and tripropyl lead both blocked the pathway by which glucose is oxidized from pyruvate to high-energy phosphate compounds. Glycolysis to lactic acid was not inhibited. Similar effects were produced by triethyl lead, but tetramethyl and tetrapropyl lead did not affect glucose metabolism except at high concentrations.

Brain slices prepared from rats previously treated with tripropyl lead showed marked inhibition of glucose metabolism, whereas no inhibition occurred in brain slices from rats treated with tetrapropyl lead. Brain slices prepared from rats showing signs of poisoning by trimethyl lead also failed to inhibit glucose metabolism. This seeming discrepancy may be due to the high solubility of trimethyl lead in water so that the compound is distributed in the medium at too low a concentration to produce any effect. The low toxicities of tetramethyl lead and tetrapropyl lead are ascribed to the slowness of their conversion in vivo to tri- compounds as compared with tetraethyl lead, which is converted rapidly to the triethyl compound.

A warning is given that it should not be too readily assumed that these findings in experimental animals can be applied to man.

W. K. S. Moore

Forensic Medicine and Toxicology

757. Modification of Agar Diffusion Technic for Use in Identification of Blood Stains

F. INNELLA, M. L. PANSEGRAU, and W. J. REDNER. American Journal of Clinical Pathology [Amer. J. clin. Path.] 36, 322-327, Oct., 1961. 5 figs., 18 refs.

A simple modification of the Ouchterlony plate technique which, it is claimed, will identify human bloodstains up to 5 years old even after prolonged heating at 200° C., is described. The antihuman serum used is a standard serum employed as a Coombs-test reagent and is prepared by immunizing rabbits with a euglobulin fraction of human serum adsorbed on to latex particles. In preliminary experiments this was shown to be capable of detecting human serum in dilutions of up to 1:40,000 and to give cross-reactions with monkey serum only, being otherwise specific. This heterologous activity may be removed by absorption with successive aliquots of monkey serum rendering the antihuman test serum completely specific but reducing its reactivity markedly.

In practice the procedure is simple; a small disk of the stained cloth is removed, a punch or cork-forer being used, and is inserted into one of a series of wells in the agar plate which surround a central well containing the antihuman serum. Control disks of unstained cloth and of bloodstains of various species occupy the remaining wells, and after moistening dry stains with saline the plates are incubated for one to 5 days, after which time no further change occurs. The problems posed by cross-reactivity of sera in this field are discussed.

Gilbert Forbes

758. Endemic Fluorosis: with Particular Reference to Fluorotic Radiculo-myelopathy

A. SINGH and S. S. JOLLY. Quarterly Journal of Medicine [Quart. J. Med.] 30, 357-372, Oct., 1961. 10 figs., 38 refs.

The authors report from Patiala Medical College a 5-year study of endemic fluorosis which occurs in certain districts of the Punjab, a northern state of India. The condition, which usually results from the ingestion of large quantities of fluoride-rich water over a number of years, was studied in 60 patients (49 men and 11 women) who were seen during the period 1956 to 1960 and in all of whom the diagnosis was confirmed radiologically. Their ages ranged from 28 to 80 years, most of them were engaged in active manual work, and all had lived for over 20 years in an endemic area in some parts of which the subsoil water and soil contained fluorine in a concentration as high as 14 parts per million.

Fluorosis produces a fairly well-defined clinical condition involving particularly the teeth, skeleton, and nervous system. In this series the dental changes consisted of loss of normal enamel translucency, mottling, and later pitting of the teeth. The skeletal changes included irregularity in bone contours and some bones were abnormally heavy owing to excessive deposition of

fluorides. Calcification in muscles and tendons was also seen. The cervical spine often showed the greatest skeletal changes. Radiological examination revealed osteosclerosis and irregular osteophyte formation and also the calcification in muscles and tendons. The histopathology of the bones was studied in 7 cases, in 6 by open bone biopsy of the tibia or iliac crest and in one at necropsy. Compact bone showed disordered lamellar orientation and a poorly formed Haversian system. In the spongy bone, pieces of osteoid tissue were found among normal bone trabeculae. Chemical analysis of bone ash showed a fluoride concentration varying from 70 to 680 mg, per 100 g, of bone ash, compared with the normal figure of 110±20 mg. per 100 g. The neurological features included muscle wasting, acroparaesthesiae, root pains, and sensory disturbances. In contrast to the findings in industrial and experimental fluorosis, renal function tests did not reveal any significant abnormality.

In the authors' opinion, the hot climate of India necessitates the drinking of large quantities of water and so increases the amount of fluoride ingested in endemic areas, and also raises its concentration; significantly high levels of fluoride were found in the blood and urine. The authors consider that the much better nutritional state in countries such as the U.S.A., where equally high fluoride contents occur in water and soil, is a factor affording protection against the crippling effects of fluorosis as seen in India.

P. T. Main

759. Amino-aciduria in Salicylate Intoxication

B. F. Andrews, O. C. Bruton, and E. C. Knoblock. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 411-414, Oct., 1961. 1 fig., 20 refs.

The finding of amino-aciduria in 4 children aged $2\frac{1}{2}$ to 3 years suffering from salicylate intoxication is reported from the Walter Reed General Hospital, Washington, D.C. On admission the patients' blood salicylate level was 41 to 59 mg. per 100 ml. and the total 24-hour urinary excretion of salicylate was 318 to 715 mg. The total 24-hour urinary excretion of α -amino nitrogen was 162 to 340 mg., average 15.7 mg. per kg. body weight per 24 hours compared with 3.1 mg. in controls. The highest increase was in sulphur-containing amino acids, the amino-aciduria thus closely resembling that in hepatic injury and differing from the aciduria seen in other forms of intoxication. It is suggested that the toxic action of salicylate is due to the ability of the drug to block the production of high-energy phosphate.

V. J. Woolley

760. Clinical Pharmacology of Systemic Antidotes. [Review Article]

A. K. Done. Clinical Pharmacology and Therapeutics [Clin. Pharmacol. Ther.] 2, 750-793, Nov.-Dec., 1961. 5 figs., bibliography.

Anaesthetics

761. Indirect Estimation of Arterial pCO₂
E. A. Cooper and H. Smith. *Anaesthesia* [Anaesthesia]
16, 445-460, Oct., 1961. 5 figs., 16 refs.

Four methods for the indirect estimation of arterial carbon dioxide tension (pCO₂) during anaesthesia with intermittent positive pressure respiration have been evaluated by the authors at the Royal Victoria Infirmary, Newcastle upon Tyne. Blood from the lobe of the ear was collected after local vasodilatation had been produced with histamine cream and by vigorous rubbing, samples of arterial blood being collected simultaneously. The pH of the blood was estimated by the micro-Astrup method and the pCO₂ determined by interpolation. Good correlation was found in 8 of the 10 patients so examined; in the remaining 2 cases the pCO2 of ear blood was higher than that in arterial blood owing to autonomic disturbances producing alterations in the peripheral circulation. For the second method venous blood from the back of the hand was similarly compared with arterial blood; here the correlation was not so good as with ear blood, although on the other hand autonomic disturbance did not produce such a gross error.

In performing the third method samples of rebreathed gas were taken by equilibrating the gas mixture in the lungs with that in a reservoir bag and the contents of this bag then analysed for carbon dioxide content by an infra-red gas analyser. Correlation with the interpolated pCO₂ of arterial blood showed a mean difference of only 5 mm. Hg, although the standard deviation was 3 to 4 mm. Hg. Lastly, in the fourth method samples of end-tidal gas were compared with samples of rebreathed gas. This method was found to give less accurate estimates of arterial pCO₂, although the error was fairly constant for a particular subject in particular circumstances.

The authors conclude that the method using rebreathed gas is best for clinical purposes in that it is simple and reliable and has an adequate degree of accuracy.

J. V. I. Young

762. Gastric Inflation in Relation to Airway Pressure. [In English]

H. Ruben, E. J. Knudsen, and G. Carugati. Acta anaesthesiologica Scandinavica [Acta anaesth. scand.] 5, 107–114, 1961. 2 figs., 1 ref.

The minimum pressure necessary to inflate the stomach was investigated [at the Finsen Institute, Copenhagen] in 20 patients. Static pressures were produced after insufflation through a mask or a tube, ending in the upper pharynx or just above the cardia. With the head in the normal position, pressures below 15 cm. $\rm H_2O$ rarely produced insufflation of the stomach, while pressures exceeding 25 cm. $\rm H_2O$ in most patients did so. Forcefully pushing back on the anterior surface of the neck against the tracheal cartilages always increased inflation pressure to above 50 cm. $\rm H_2O$.

These data suggest that when performing artificial respiration by bag and mask or by expired air, relatively small inflation pressures should be used to avoid an unnecessary rise of the pressure in the pharynx. As the pressure fall is greater through the nose than through the mouth, expired-air resuscitation is less apt to produce gastric inflation when performed by the mouth-to-nose than by the mouth-to-mouth technique.—[Authors' summary.]

763. Concentrations of Lignocaine in the Blood after Intravenous, Intramuscular, Epidural and Endotracheal Administration

P. R. Bromage and J. G. Robson. Anaesthesia [Anaesthesia] 16, 461-478, Oct., 1961. 8 figs., 17 refs.

This paper from McGill University and the Royal Victoria Hospital, Montreal, describes an investigation into the rates of absorption of lignocaine into the blood following various methods of administration and into the blood lignocaine levels associated with toxic signs. The concentration of lignocaine was measured in duplicate 5-ml. samples of venous blood from 65 patients at intervals after the administration of lignocaine by intravenous, intramuscular, or epidural injection or by endotracheal spray. Details of the method used are given.

To 7 patients anaesthetized with thiopentone, nitrous oxide, and oxygen, lignocaine was given intravenously in doses of 9.7 to 16.3 mg. per kg. body weight at infusion rates varying between 9.3 and 100 mg. per minute: Acute toxicity, manifested by falling blood pressure and hypoventilation, appeared at blood lignocaine levels above 10 µg. per ml., but not from infusion rates below 0.3 mg. per kg. per minute unless previous accumulation -had occurred. In 14 similarly anaesthetized patients 2% lignocaine given intramuscularly produced a peak in blood concentration between 15 and 35 minutes later; but although doses greater than 1.3 mg. per kg. would be likely to produce blood levels above 10 μ g. per ml., no signs of toxicity appeared, though a small fall in blood pressure occurred in one patient with a concentration of $13.25 \mu g$, per ml. In 27 patients an epidural block was performed with 2% lignocaine in doses of 3.5 to 10.5 mg. per kg. In 12 cases 1:400,000 to 1:200,000 adrenaline was added as a vasoconstrictor. Maximum concentrations appeared in the blood 18 to 23 minutes later and were significantly higher in those not receiving adrenaline, while the quality of nerve blockade seemed more intense and prolonged where adrenaline was added. Systemic absorption therefore did not enhance segmental analgesia, though high blood concentration may lead to overdosage. In 12 patients anaesthetized with thiopentone, topical analgesia of the trachea with 4% lignocaine in doses of 3.5 to 10.5 mg, per kg, produced peak blood levels between 5 and 23 minutes later. Though the blood concentration rose to 10 μ g. per ml. in one

patient no toxic signs were observed in any. Statistically, a rise in blood concentration above 10 μ g. per ml. could result from a dosage of 6 mg. per kg., which should not be used.

From discussion of the results of this investigation and other published work it is concluded that toxic symptoms following the intravenous injection of lignocaine depend on the rate of administration and elimination and the size of the patient as well as on absolute toxicity, and rates of 0.3 mg, per kg, per minute are tolerable for 30 minutes, the rise in blood concentration remaining below 6 to 7 μ g. per ml. Higher blood concentrations following intramuscular administration appear to be tolerated without toxic symptoms appearing, possibly because the level is achieved more slowly. The margin of safety is small, however, a small increase in the dose producing a disproportionate increase in the blood concentration of the drug. With epidural block excessive concentrations are not likely to be reached with doses below 7 to 8 mg. per kg. for plain lignocaine or below 10 to 11 mg. per kg. when 1:200,000 adrenaline is added, unless accidental direct injection into the blood stream occurs. The variability in the rate of rise of blood lignocaine concentration following topical analgesia probably reflects differing rates of absorption from different parts of the respiratory tract, alveolar absorption being very rapid and tracheal absorption less so. It appears, however, that 4% lignocaine in doses up to 6 mg. per kg. may be sprayed into the trachea without causing a dangerous rise in blood level. The likelihood of achieving general analgesia with a concentration of 1 5 μ g, per ml. would appear to be good; this is about one-half the concentration likely to produce toxic symptoms, giving a relatively small margin of safety.

, \ Raymond Vale

764. Laboratory and Clinical Comparisons of Halothane and the Azeotrope Halothane-Ethyl Ether

C. R. STEPHEN, V. MEDRADO, P. DUVOISIN, and K. D. HALL. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 509-520, Sept.-Oct., 1961. 9 figs., 6 refs.

A laboratory and clinical comparison of the azeotrope; halothane—ethyl ether, and halothane indicates that both drugs act in a similar manner, although the azeotrope is somewhat less potent, according to volumes per cent administration. Clinical administration of the azeotrope is not associated with any specific advantages to the patient or the anesthesiologist.—[Authors' summary.]

765. A Preliminary Report on the Use of Intramuscular Methohexital Sodium ("Brevital") for Pediatric Anesthesia

J. R. MILLER, V. K. STOELTING, and M. W. DANN. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 573-577, Sept.-Oct., 1961. 6 refs.

A study of the intramuscular use of methohexitone sodium ("brevital") in paediatric anaesthesia is reported from Indiana University School of Medicine, Indianapolis. The patients studied were undergoing a variety of surgical operations, and ranged from newborn infants

to children of 16 years of age. Most of the patients were premedicated with morphine (1 mg. per year of age) or pethidine (1 mg. per lb. or 2.2 mg. per kg.) together with atropine or scopolamine. Methohexitone as a 2% solution in normal saline was used to provide basal narcosis; this was injected intramuscularly in a dose of 4 mg. per lb. (8.8 mg. per kg.) body weight. The onset of sleep usually occurred in 2 to 6 minutes, and when methohexitone was given alone sleep lasted for 30 to 45 minutes. If the child was not asleep in 10 minutes an additional dose of 3 mg. per lb. (6.6 mg. per kg.) was given. Intramuscular injection of methohexitone was found to be most effective in patients weighing from 30 to 60 lb. (13.6 to 27.2 kg.).

The authors employed a variety of anaesthetic agents following this form of basal narcosis. No important complications attributable to the methohexitone were noted during maintenance of anaesthesia.

Mark Swerdlow

766. Intramuscular Trimeprazine Tartrate: a Clinical Trial of Its Use as a Pre-operative Drug

J. L. SIMCOCK. Anaesthesia [Anaesthesia] 16, 483-488, Oct., 1961. 7 refs.

From the Opotiki Hospital, New Zealand, a clinical trial of 1% trimeprazine tartrate given intramuscularly as a preoperative drug in 380 cases is reported. The dosage was 5 mg. per stone (0.785 mg. per kg.) body weight for children under the age of 12 years, and 4 mg. per stone (0.628 mg. per kg.) above that age. When pain was present pethidine in doses of 10 mg. per stone (1.57 mg. per kg.) was given and, as an antisialogogue, hyoscine in doses of 1/500 grain per stone (0.04 mg.) for adults and 1/200 grain per stone (0.05 mg.) for children was given 90 minutes before induction. The patients were assessed as stuporose, asleep, dozing, drowsy, alert, or apprehensive, and the degree of cooperation during induction with nitrous oxide was noted.

No patients were classified as stuporose or apprehensive and over two-thirds were either dozing or drowsy. Adults held the face mask in position until unconscious and only 4 out of 236 required persuasion to do this. Of 144 children under 12 years old in whom anaesthesia was induced with nitrous oxide introduced under a "perspex" dome, only 13 attempted to resist, 2 of them seriously. These two had had their premedication less than 30 minutes before induction. A stage of excitement was seen in 54 patients, in 15 of whom some restraint was required. In 3 patients pain at the site of injection persisted for 48 hours, but no other effect such as fall in blood pressure or respiratory depression was seen and postoperative recovery of consciousness was not delayed. Postoperative vomiting was rare and there was no restlessness in the absence of pain and no pulmonary complications. Most of these patients received their premedication 1 to 12 hour before induction; where this interval was smaller, sedation and cooperation were diminished, but extension of the interval up to 2½ hours made no difference to sedation or cooperation.

The author discusses the results and considers them more predictable than when the oral route is used.

Raymond Vale

Radiology

767. Double Contrast Sinography
H. D. C. Bell. British Journal of Radiology [Brit. J. Radiol.] 34, 630-634, Oct., 1961. 10 figs.

A method of double-contrast sinography is described in this paper from the Royal Infirmary, Wigan, Lancashire. The value of the method is illustrated with 6 cases and the hazards are discussed. The apparatus consists of the insufflation bag from an anaesthetic machine, a 50-ml. syringe, and a catheter, which are connected to a three-way tap. The patient is placed on the x-ray table in an appropriate recumbent position. The catheter is introduced into the sinus, a close but not occlusive fit being made. Under screen control "urografin" (sodium and methylglucamine triiodo-- benzoate) is injected until the abscess cavity, if present, is just beginning to fill or until no further filling of the sinus tract or its ramifications is seen. Then carbon dioxide is injected until urografin starts to reflux down the sinus tract. Films are taken in various positions.

The method is said to give better demonstration of abscess cavities and their contents, of the sinus tract, of surrounding viscera, and of communications with bone or viscera. No complications were encountered in this series. The use of readily soluble contrast media (urografin and carbon dioxide) minimizes the risk of contrast embolism, but the possibility of septic emboli and the introduction of secondary infection does exist.

Arnold Appleby

768. Value of Laryngography in Vocal Cord Tumors J. Medina, W. B. Seaman, P. Carbajal, and D. C. Baker. *Radiology* [*Radiology*] 77, 531-542, Oct., 1961. 16 figs., 14 refs.

A review of the results of 100 laryngographic examinations performed at the Columbia-Presbyterian Medical Center, New York, confirmed the value of this technique in that it gave a higher proportion of successful diagnoses, compared with conventional methods not using contrast media. In performing the procedure thorough anaesthetization of the larynx and trachea is obtained by topical spraying with 2 to 4% lignocaine, followed by the direct instillation of a few ml. of this drug into the trachea through a curved metal cannula. Thereafter 5 to 15 ml. of "dionosil oily" is injected into the larynx and hypopharynx, and multiple spot films are taken in the frontal and lateral positions during quiet respiration, phonation, and performance of the Valsalva and modified Valsalva manœuvres. The normal anatomical and physiological features and variations are discussed and the pathological appearances, with special emphasis on tumours of the vocal cords, described. Benign polyps of the vocal cords were demonstrated in all of 8 such cases in the series. In regard to the 19 patients with malignant neoplasm of the vocal cords examined it is noted that of the 9 with subglottal extension of the tumour definite evidence of this was obtained in only one case by direct laryngoscopy, but in 8 by laryngography and the condition strongly suspected in the ninth.

B. Golberg

769. Laryngeal Pathology on the Conventional Roentgenogram of the Chest: Diagnostic and Prognostic Significance

S. M. UNGER and B. ROSWIT. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 661-668, Oct., 1961. 6 figs., 12 refs.

In the interpretation of routine chest radiographs, careful scrutiny of the air column overlying the cervical spine can be most revealing. Carcinoma of the laryngopharynx or trachea as well as vocal-cord paralysis secondary to recurrent laryngeal nerve involvement may be detected. It is important to know, however, whether the exposure was made during inspiration or expiration, the appearance of the larynx and glottis varying greatly in these two phases. In inspiration the aperture of the glottis is wide with no visualization of the ventricles: in expiration the glottis is reduced to a narrow slit and the ventricles are filled with air. If the patient is at the end of the inspiratory phase or at the beginning of expiration, he will suddenly stop breathing and thereby carry out a modified Valsalva manœuvre; the radiograph will show the vestibule, ventricles, glottis, and trachea. Illustrative examples of the value of scrutiny of the air John H. L. Conway-Hughes column are given.

770. The Radiological Appearances of the Chest in Polycythaemia Vera

R. G. PITMAN, R. E. STEINER, and L. SZUR. *Clinical Radiology [Clin. Radiol.*] **12**, 276–285, Oct., 1961. 9 figs., 16 refs.

The authors have studied the radiological changes in the lungs in 86 cases of polycythaemia vera at Hammersmith Hospital, London. All these cases were treated with radioactive phosphorus (³²P), and in all of them postero-anterior chest radiographs were taken at intervals of 3 to 12 months during the period of observation, which varied between one and 11 years.

Abnormal distension of the pulmonary vessels was found in 51 patients, and 21 had small segmental areas of consolidation, atelectasis, or fibrosis thought to have resulted from infarcts. Cardiac enlargement was present in 21 patients, 14 of whom had hypertension. Five patients had fractured ribs, and radiological evidence suggestive of myelosclerosis was observed in 3 cases.

A statistically significant correlation was found between the packed cell volume and the pulmonary vascular dilatation, and the changes in both during treatment were parallel. There was similar correlation between the evidence of infarction and the packed cell volume. Pulmonary septal lines were not found, which helps to differentiate the pulmonary vascular distension in these cases from that due to left heart failure. Cor pulmonale in chronic bronchitis may produce an identical pattern, but pulmonary vascular dilatation due to congenital heart disease should be readily distinguished from that occurring in-polycythaemia vera.

D. E. Fletcher

771. Technique of and Indications for Cine-angiocardiography. With Reference to 100 Films. (Technique et indications de la cinéangiocardiographie. A propos de cent films)

M. MOUQUIN, P. BRUN, and H. GESCHWIND. Archives des maladies du cœur et des vaisseaux [Arch. Mal. Cœur] 54, 961-969, Sept. [received Nov.], 1961. 5 figs.

The authors describe a technique of cine-angiocardiography with a 16-cm. image intensifier and a 16-mm. cine-camera with a maximum speed of 25 frames per second, limiting the time of exposure to 10 to 20 seconds. Several copies are made of each sequence and then joined together so that by means of a variable-speed projector with stop and reverse the films can be viewed at least a dozen times, experience having taught the authors the absolute necessity of close and prolonged study. Further studies are then made of single shots and then of groups of 3 or 4 shots which are projected simultaneously so that each frame can be compared with those immediately preceding and following.

The authors maintain that the indications for cineangiocardiography are legion, the only limitation being the relatively small field size. E. Giordani

772. Study of the Pulmonary Vessels in Mitral Stenosis by Thoracic Radiography. Comparison of Radiological and Haemodynamic Findings. (Étude des vaisseaux pulmonaires dans le rétrécissement mitral par la radiographie thoracique. Confrontation radio-hémodynamique)

P. CALAZEL, R. BOLLINELLI, J. C. LIGOU, and J. CASSAGNEAU. Archives des maladies du cœur et des vaisseaux [Arch. Mal. Cœur] 54, 970–984, Sept. [received Nov.], 1961. 6 figs., 14 refs.

Analytical study of the pulmonary vessels in a normal radiograph of the chest reveals that nearly all the vascular opacities are arterial. The arteries appear as rectilinear opacities rapidly decreasing in size as they extend from the hilum to the periphery. They are more distinct in the upper lobes, and at the bases their course is uncertain, being frequently obscured by bronchial opacities and, in certain pathological conditions, by venous shadows. Only when the arterial shadows are very opaque, dilated, and numerous is it obvious that they are pathological. The presence of venous opacities in a chest is nearly always pathological. These opacities, however, are difficult to recognize. They are sinuous, with fading edges, often larger than the corresponding arterial shadows and difficult to trace for any distance. Sometimes they can be seen enlarging as they approach the hilum, but the surest sign is their convergence towards the left auricle. Finally, there are peripheral opacities difficult to interpret and probably of complex origin.

As a result of such radiological analysis in 85 cases of mitral stenosis the authors have been able to identify various types of congestion. (a) Purely arterial hypervascularity. This was rare and accounted for only 4% of cases. (b) Venous or veno-capillary hypervascularity, accounting for 24% of cases. (c) Global pulmonary hypervascularity, which was seen in 64% of cases and consisted in varying degrees of arterial hypervascularity superimposed on a basic venous type of congestion. It was found that, with a few exceptions, the cases in each radiological group had similar haemodynamic findings.

773. Cardiac Laminagraphy

K. D. McGinnis, W. R. Eyler, and H. Alvarez Jr. Radiology [Radiology] 77, 553-563, Oct., 1961. 14 figs., 13 refs.

In the standardized procedure for cardiac laminagraphy which has been evolved at the Henry Ford Hospital, Detroit, and is here described, the left lateral decubitus position is used, as it is easily duplicated at subsequent examinations and the positions of the cardiac valves maintain a relatively constant relationship to the sagittal plane. Beginning at this plane 4 sections at intervals of 1 cm. are taken to the left for the evaluation of the valves, this procedure being modified as required if other areas have to be examined. A single-section technique is used. It was found helpful to divide the lateral cardiac laminagraphic silhouette by a diagonal line extending from the intersection of the tangents of the anterior and inferior cardiac surfaces to the posterior surface of the left main bronchus. This "bronchophrenic" line is usually anterior and superior to the mitral valve and posterior and inferior to the aortic valve, being so positioned in 93 out of 102 cases of calcification analysed.

In the series described, calcifications were found in 39 mitral valves, this number being made up of 30 out of 99 cases of mitral disease and 9 cases of combined mitral and aortic disease. Calcification was also found in 66 aortic valves, including 54 out of 64 cases of aortic valvular disease and 12 out of 30 with combined aortic and mitral involvement. One case of calcification of the pulmonary valve was seen. Calcification was also seen in the pericardium (3 cases), coronary arteries (3 cases), intraluminally (one case of calcified thrombus), in the ventricular myocardium (in an old aneurysm), and in a ring above the aortic valve in one case. Cardiac laminagraphy is of value in confirming fluoroscopic findings and also facilitates the identification of multiple calcifications, while at the same time providing a permanent record of the site and amount of such calcification. The radiation dose is relatively low. B. Golberg

774. The Solitary Dense Vertebral Body
J. M. DENNIS. Radiology [Radiology] 77, 618-621,
Oct., 1961. 5 figs., 3 refs.

While osteosclerosis is frequently observed in several lower dorsal or lumbar vertebral bodies, its limitation to a single vertebral body is a rather unusual finding. This report from the University of Maryland, Baltimore, concerns 16 examples of a solitary dense vertebral body collected by the author; of these, 8 were due to focal Paget's disease, 5 to Hodgkin's disease, one to reticulum-cell-sarcoma, and 2 to metastatic cancer. Other causes of such lesions, although recognized in the literature, were not encountered.

Solitary manifestations of Paget's disease occur in about one out of 10 cases, the spine being most commonly affected. Atrophy of the spongiosa produces coarse vertical trabeculation or subcortical sclerosis, and in this series the appearances were typical of those found elsewhere in the skeleton. A double contour or "picture frame" may result from subcortical sclerosis. Enlargement of the affected vertebral body was noted in 6 of the 8 cases, and in 4 cases confirmatory evidence of the diagnosis was found elsewhere in the skeleton.

Post-mortem evidence of bone involvement in lymphomatous conditions, including Hodgkin's disease and reticulum-cell sarcoma, is found in approximately 50% of cases, but in only about half of these are there radiological signs of such involvement. Haematogenous spread commonly produces multiple bone foci often affecting the vertebral bodies. Localized involvement of a vertebral body was found to be associated with invasion of the periosteum and bone from neighbouring lymph nodes which had been involved by the disease. At operation these were surgically inseparable from the affected vertebral body. These bodies presented a dense and amorphous appearance, in 2 cases accompanied by evidence of extrinsic osteoblastic activity, with irregular bony proliferation externally along one or more margins. The author regards this appearance as being characteristic of a lymphoma.

Osteoblastic metastases in the spine usually involve several vertebrae and are commonly secondary to carcinoma of the prostate, although there may be other causes. Limitation of the lesions to a single vertebral body was found in 2 cases. The increase in density was like that seen with widespread metastases and consisted of patchy and confluent areas; it was therefore less homogeneous than that found in the other conditions described. The primary lesions in these cases were carcinoma of the nasopharynx and of the colon.

R. O. Murray

775. The Incidence of Urographic Findings in Tumours of the Urinary Bladder

H. Braband. British Journal of Radiology [Brit. J. Radiol.] 34, 625-629, Oct., 1961. 6 refs.

A statistical evaluation of 1,000 cases of proven tumour of the bladder as recorded in the Bristol Bladder Tumour Registry since 1950 has been carried out. In order to obtain more detailed information, 100 cases of bladder neoplasm with positive x-ray findings were reviewed.

Of the total of 1,000 cases, urography was performed in 732. The most frequent abnormal urographic finding was a filling defect in the bladder (36.8% of the 732 cases); changes in the upper urinary tract were seen in 19.5%, and 6.3% of cases showed the combination of a filling defect in the bladder shadow and involvement of the upper urinary tract.

The statistical analysis and the review of 100 of the cases with positive urographic findings have permitted of several conclusions. (1) Urographic examination is worth while for the diagnosis of vesical neoplasms and the demonstration of their effects on the upper urinary tract, provided there is no evidence of renal failure and there has been no bleeding for at least 48 hours. (2) Attention should be paid to the lesser degrees of involvement of the upper urinary tract, such as stasis in the lower part of the ureter, and not only to hydronephrosis and loss of excretory function. (3) The spread of a bladder tumour may occur in the wall only, so that no filling defect may be visible, but changes such as thickening of the wall, deformity of the outline, or loss of contractility may be detectable. The post-micturition film is of value particularly for demonstrating loss of or decrease in contractility. (4) The presumption that papillomatous growths are in most cases benign is erroneous; of 916 tumours which were carefully graded histologically, only 14 (1.5%) were simple benign papillomata, all the rest showing malignancy of some grade. Arnold Appleby

.776. Cineurethrography and Voiding Cinecystography, with Special Attention to Vesico-ureteral Reflux

K. E. Gross and S. S. SANDERSON. *Radiology* [Radiology] 77, 573-585, Oct., 1961. 13 figs., 19 refs.

From the Mary Bridge Children's Hospital, Tacoma, Washington, the authors describe the use of cine-urethrography in the investigation of lower urinary tract disease. with particular reference to vesico-ureteric reflux. The apparatus consists of a 16-mm. synchronized cinecamera with an 8-inch (20-cm.) amplifier and a film exposure speed of 7.5 frames per second. It was calculated that the average exposure dose to the gonads was 1.1 r. plus or minus 25%. The opaque material was one of the usual water-soluble media diluted to a 15% solution of iodine, with an additional 5 ml. each of hypoand hyper-baric lipiodol to create an "opaque sandwich", and it is introduced through a small catheter, the films being taken at the time of introduction and in bursts so as to reduce unnecessary dosage of radiation. A delay of about 3 hours is allowed because of reported increased incidence of reflux after delay, though reflux may occur at any time. The patient then attempts initiation and cessation of voluntary micturition. During micturition the urethral portion of the bladder, the dome, and the lower ureters are all visualized. Male patients are placed in the steep right oblique position with elevation of the flexed right leg, while in the female frontal, and if possible, oblique views were obtained. However, trials showed that for both sexes the erect position is preferable if this is possible. Recording on film is continued throughout micturition, with a final scan of the ureters and kidneys, this having previously been done at least once before and during bladder filling and also in the delay period.

As stated, vesico-ureteric reflux may occur at any time during the examination and is completely unpredictable; it was seen in 47% of this series of 83 cineradiographic studies. The high incidence is attributed to the selection of likely cases, based on clues seen in the excretory pyelo-

grams. In order of importance these clues were (1) minimal dilatation of the lower third of the ureter with uretero-vesical "narrowing"; -(2) the presence of a "bladder mucosal saccule"; (3) the presence of the "notch sign"; (4) uretero-pelvic obstruction or unexplained calicectasis, pyelectasis, or ureterectasis; (5) small or suspected hypoplastic kidney; and (6) malposition of the ureteral orifice, duplication of the ureter, or ectopic kidney. In the authors' experience cinecystography and voiding urethrography are indicated in the presence of any of these signs. The most positive indication of probable reflux is a small protrusion beyond the bladder shadow situated adjacent to the vesicoureteral iunction. This is thought to be due to displacement of the former intravesical ureter to an extravesical position. This portion of the ureter is incapable of propelling urine and acts only as an obstructing segment, thus explaining the narrowing seen. In addition, the bladder mucosa herniates at this site owing to breakdown of the longitudinal muscle fibres. The "notch sign" or the "mucosal hernia" are virtually pathognomonic of reflux.

The authors have found cine-urethrography also of value in distinguishing between organic and functional deformities of the urethra, and between true achalasia of the ureter and localized ureterectasis due to reflux.

B. Golberg

RADIOTHERAPY

777. The Treatment of Malignant Tumours of the Skin of the Face. (Die Behandlung bösartiger Hautgeschwülste im Gesicht)

K. Nehls. Strahlentherapie [Strahlentherapie] 116, 214-226, Oct. [received Dec.], 1961. 10 refs.

This is a report on 238 cases of malignant disease of the skin of the face seen since 1945 at the University Ear, Nose and Throat Clinic, Greifswald. Such a department, equipped for both surgery and radiotherapy, is felt to be very suitable for this type of case, as the balance can be fairly held between the two alternative means of treatment. Detailed lists are given of the results obtained in various sites according to histological type and mode of treatment.

There were 102 tumours of the pinna. Surgery is the treatment usually favoured, but the author makes a plea for radiation. Radium is useful, but the technique of choice is short-distance Chaoul x-ray therapy (focusskin distance 5 cm.). This carries a minimal risk of perichondritis and is therefore superior to deep x rays. Moreover, the cosmetic results are good, even if some cartilage has to be subsequently removed. For small growths of the anterior or posterior surface or of the free edge of the pinna a daily dosage of 400 r. to a total of 6,000 to 7,000 r. is advised. If cartilage, the external auditory meatus, or the middle ear is involved radical surgery is advised. For tumours involving the auricle and adjacent skin, the prognosis is worse for reasons unknown. Small superficial growths of the lip and nose are also best treated by radium (needle) or Chaoul therapy. Needling is preferred for infiltrating growths.

Surgery is advised for secondary nodes. Similar techniques apply to other parts of the face, and the prognosis there is relatively favourable.

J. Walter

778. The Treatment of Advanced Carcinoma of the Bladder: a Report on 89 Patients Treated with Either Two-million-volt or Cobalt-60 Therapy or with a Combination of This Type of Irradiation and Surgery

R. GUTTMANN and A. BAUZA. Radiology [Radiology] 77, 465-471, Sept., 1961, 22 refs.

Between January, 1951, and January, 1960, at the Francis Delafield Hospital, New-York, 89 patients with cancer of the bladder were treated by radiotherapy, 79 by 2-MeV, x-ray therapy or radioactive cobalt (60Co) therapy, while 10 received in addition surgical treatment. Of the 79 patients treated by radiotherapy only, 42 had had some form of previous therapy and 14 had distant metastases. Patients with advanced recurrent carcinoma or those with metastases received 3,000 r. in the course of 3 weeks through large opposing pelvic fields. The others received 4,000 to 6,000 r. over 4 to 6 weeks, 2 MeV. being given through fixed fields or by full rotation or anterior scanning on the 60Co unit, 200 r. (reduced to 100 r. if not tolerated) being delivered to the tumour daily. Local and general tolerance of this dosage was good.

Of 18 patients treated to a limited extent, all except 2-died within one year; decrease in the amount of haematuria was the most impressive symptomatic improvement in this group. Of 53 patients with radical healing 6 were alive after 5 years and free of disease, 9 further patients survived over 3 years, 2 died without evidence of disease, 5 are alive without evident disease; and 2 have residual tumour. Of these 53 patients 4 were operated upon after therapy. Although in some cases surgery was difficult, there were no severe complications. One patient was operated on after only half the treatment had been given, and at that time the tumour had completely disappeared. Examination of the specimen in another case showed the tumour to be well walled off by fibrous tissue.

In view of the fact that some patients who had been free of disease for one or 2 years returned with widespread recurrences the authors devised a new programme. In this, 3,000 r. is given preoperatively and cystectomy then performed 2 weeks after the end of therapy. If the disease is not confined to the bladder a further 3,000 r. is given postoperatively. So far 10 patients have been treated in this way and in 5 of these no residual tumour was found in the operated specimen. Of these patients, who all benefited from radiotherapy and who all had papillary or transitional-cell carcinoma of various grades, 6 are alive 2 to 5 years after treatment. The authors suggest that this method ought to be considered as a worthwhile procedure in patients with advanced bladder cancer without distant metastases and who are in good general condition. I. G. Williams

779. Radioactive Isotopes in Radiotherapy (Part Two) K. E. HALNAN. Clinical Radiology [Clin. Radiol.] 12, 311-323, Oct., 1961. Bibliography.

ABSTRACTS OF WORLD MEDICINE

Vol. 31 No. 4 April, 1962

Pathology

780. A Comparison of Laboratory Methods for the Control of Anticoagulant Therapy with Prothrombinopenic Agents. I. The Quick One-stage Procedure, the Prothrombin and Proconvertin Test and the One-stage Determination of True Prothrombin Activity

T. RODMAN, B. H. PASTOR, and K. C. FAWCETT. American Journal of Medicine [Amer. J. Med.] 31, 547-554, Oct., 1961. 3 figs., 8 refs.

An investigation was carried out at the Veterans Administration Hospital, Philadelphia, to assess the validity of some of the objections to the standard Quick one-stage procedure as a method of controlling anticoagulant therapy. The Quick test performed with standard commercial thromboplastin was compared with a method in which a thromboplastin said to be free from Factor-VII activity was used, with the P and P test of Owren, and with true prothrombin determination. The anticoagulant used was bishydroxycoumarin, and the results reflected the fact that the four tests each measured different coagulation factors which were all being depressed in varying degree at different times. The authors point out that it is not known which factor or factors must be depressed for effective anticoagulation, nor is it known which factor or factors must be depressed to result in excessive bleeding. It is therefore impossible to decide which test will provide the most accurate control of clinical anticoagulant treatment, but they conclude that the simple Quick one-stage procedure, properly performed, is a satisfactory method for general use in the light of the present incomplete knowledge of anticoagulant mechanisms. A. Brown

781. A Comparison of Laboratory Methods for the Control of Anticoagulant Therapy with Prothrombinopenic Agents. II. Problems Encountered in the Laboratory Control of Anticoagulant Therapy with the One-stage Determination of Prothrombin Complex Activity

T. RODMAN, B. H. PASTOR, and B. L. HOXTER. American Journal of Medicine [Amer. J. Med.] 31, 555-563, Oct., 1961. 7 figs., 8 refs.

The Quick one-stage procedure is probably the most widely used test for the control of anticoagulant therapy, but it has often been criticized in clinical practice. The authors set out to assess the effects of variations in materials and techniques; different thromboplastin preparations were compared, dilution curves and diluents were studied, and variations in handling of the plasma were considered. The findings indicated that the test was simple and accurate, but that errors could occur

because of the use of incorrect dilution curves for conversion of plasma clotting time to percentage of normal plasma activity. It was also found that various thromboplastin preparations might differ widely, and that prolonged exposure of the plasma and reagents to waterbath temperatures resulted in a significant fall in plasma activity. The authors conclude that the use of a highly standardized thromboplastin, together with the expression of the results in seconds (thereby excluding possible errors in dilution curves), would considerably enhance the value of the procedure.

A. Brown

782. Effects of Fractions from Leukemic White Cells on Blood Coagulation. [In English]

G. MANAI, F. MANDELLI, S. MAGALINI, and C. BORDONI. Haematologica latina [Haemat. lat. (Milano)] 4, 115–121, April-June [received Oct.], 1961. 1 fig., 7 refs.

The object of this study, which is reported from the Institute of Medical Semeiotics, University of Rome, was to prepare fractions of leukaemic leucocytes and to estimate their thromboplastic activity. The fractions studied were: (a) cellular material soluble in 0.14 M sodium chloride solution; and (b) the insoluble residue. The action of these fractions on blood coagulation was studied by determining their effect on the one-stage "prothrombin" time, recalcification time, prothrombin consumption, and the thromboelastogram. There was a negligible effect on normal platelet-rich plasma, but both fractions possessed clot-accelerating activity in heparinized plasma, platelet-poor plasma, haemophilic plasma, and Christmas-disease plasma. They behaved like weak preparations of tissue thromboplastin.

A. S. Douglas

CHEMICAL PATHOLOGY

783. Immunoelectrophoretic Studies of Cerebrospinal Fluid: Investigation in Patients with Tumour in the Central Nervous System

E. SVENNILSON, S. J. DENCKER, and B. SWAHN. *Neurology* [*Neurology* (*Minneap*.)] 11, 989–995, Nov., 1961. 5 figs., 12 refs.

At the University of Lund, Sweden, the authors examined the cerebrospinal fluid (C.S.F.) of 26 patients with cerebral tumour, 4 with pituitary adenoma, 10 with subdural and 4 with extradural tumour of the spinal cord, and one with cerebral and one with spinal arteriovenous malformation, using a modification of Scheidegger's micro-immunoelectrophoretic technique. As

controls, 30 patients with headaches, dizziness, and mild mental symptoms, but without neurological signs, were used

The total C.S.F. protein content was increased in over half of the patients with tumours, but paper electrophoresis showed no difference in its constituent fractions between patients and controls. By micro-immuno-electrophoresis, however, it was shown that 3 to 6 pathological protein fractions were present in all patients with tumours except those with pituitary adenoma, in whom no abnormality was found. Beta₁ lipoprotein was present in 28, fibrinogen in 26, and 4 different pathological β_2 fractions in one-third or more of the 40 patients with tumours of the brain or spinal cord. These protein fractions were not found in normal patients. Alpha₂ macroglobulin and the large molecular portion of γ globulin were found in increased concentration in 28 and 17 of the patients with tumours respectively.

The pattern tended to differ slightly with the type of tumour, but it is stated that investigations on a larger scale are needed before valid conclusions can be arrived at in this respect.

H. S. Schutta

784. Mellituria, a Paper Chromatographic Study H. BICKEL. Journal of Pediatrics [J. Pediat.] 59, 641-656, Nov., 1961. 3 figs., bibliography.

The results of an 8-year study of mellituria in healthy infants and children and in over 1,000 patients with various disorders seen at the Children's Hospital, Birmingham, and at the Kinderklinik, Marburg University, are reported and discussed. Each sample of urine was subjected to Benedict's reduction test and examined for fructose, galactose, glucose, lactose, and xylose by onedimensional paper chromatography under standard conditions. Measurements of sugar content on 170 samples of 24-hour urine collections from 104 full-term and premature infants showed a physiological level of mellituria with a moderate increase in 4 sugars, the maximum values for these (per 100 ml.) being 10.9±3.3 mg. for glucose, 9.1 ± 1.6 mg. for galactose, 23.1 ± 8.0 mg. for fructose, and 48.2±26.6 mg. for lactose; these raised levels persisted for 10 to 14 days. It is thought that the mellituria in the newborn is probably associated with immature functioning of the renal tubules, liver, and intestinal tract and not with the physiological aminoaciduria of infancy. In 125 healthy older children and adults sugar excretion was either very low (maximum 10 mg. per 100 ml.) or absent.

Determination of the urinary sugar levels in 1,000 selected patients with various diseases revealed 130 patients with mellituria, for which a single sugar was responsible in 114—the sugar being glucose in 77 cases, lactose in 13, fructose in 12, galactose in 11, and xylose in one—and more than one sugar was responsible in the remaining 16. The various diseases associated with mellituria are discussed. It is stated that isolated and constant mellituria is characteristic of an inborn error of sugar metabolism, whereas the symptomatic melliturias are more variable in pattern and occurrence; different sugar patterns can be distinguished in hepatic, renal, and intestinal disorders.

Finally, a sugar loading test was conducted on 45 healthy subjects and 65 patients in order to study the effect of sugar intake on sugar excretion. A mixture of glucose (400 g.), galactose (8 g.), fructose (30 g.), lactose (8 g.), and sucrose (20 g.) was given orally and samples of urine collected after 1, 2, and 3 hours. Although mild mellituria occurred in all the healthy controls, the increase in the urinary sugar levels was greater in patients with hepatic, renal, and intestinal diseases. The diagnostic value of the sugar loading test is discussed. In conclusion it is pointed out that the correlation between the chromatographic results and those of Benedict's reduction test was poor. If clinical investigation had been restricted to Benedict's test, diagnostically important melliturias, such as idiopathic galactosuria, would have been missed. Paper chromatography is therefore recommended by the author for the routine clinical diagnosis of mellituria. J. E. Page

785. Experience with the Leucine Aminopeptidase Assay S. Winsten. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 241-247, Sept., 1961. 2 figs., 5 refs.

The assay of leucine aminopeptidase in blood samples was reported by Goldbarg and Rutenberg in 1958 (Cancer. 11, 283); they suggested that this determination might be a useful aid in the diagnosis of carcinoma of the pancreas. The present author describes his experience of the assay of this enzyme in patients suffering from carcinoma of the pancreas and other malignant conditions, biopsy or necropsy material being available in each case to confirm the diagnosis. Using a modification of the method of Goldbarg and Rutenberg he found that in the normal subject the blood level of leucine aminopeptidase ranged from 50 to 200 units per ml. Levels in excess of 450 units per ml. were found in conjunction with carcinoma of the pancreas; however, similar high values were obtained in some patients with tumours of the extra-hepatic biliary system. A raised blood level of this enzyme was also observed in patients with hepatic metastases from other primary tumours.

Early in the study a relationship was noted between raised serum leucine aminopeptidase and alkaline phosphatase levels and pathological evidence of liver metastases, even in anicteric serum. With the object of establishing some objective criterion for the evaluation of cancer chemotherapy the author undertook serial assays of these serum enzymes in about 60 patients undergoing treatment. In some patients there was a very definite fall in leucine aminopeptidase activity following chemotherapy, but in the majority there was not such a dramatic response.

An increase in the leucine aminopeptidase level was also observed in patients with cholecystitis, choledocholithiasis, portal thrombophlebitis, cirrhosis, and hepatitis, and in children with biliary atresia. It would thus appear that extreme elevation of leucine aminopeptidase activity occurs in patients not suffering from carcinoma of the pancreas. The chief value of determining the blood level of the enzyme lies in the early detection of hepatobiliary disease and in the confirmation of the

presence of hepatic metastases. Serial studies may be useful in assessing the response of patients with cancer to chemotherapy.

G. Clayton

786. The Influence of Abnormal Plasma Protein on the Laboratory Tests Utilized in the Diagnosis of the Rheumatic Diseases

W. J. HAMMACK and H. L. HOLLEY. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 366-374, Sept., 1961. 3 figs., 19 refs.

The authors, working at the Medical College of Alabama, Birmingham, Alabama, have studied the incidence of C-reactive protein, L.E. cells, a positive Rose-Waaler reaction, and a positive result in the paratoluene sulphonic acid test in 5 patients with Waldenström's hyperglobulinaemia purpura, 4 with cryoglobulinaemia, one with pyroglobulinaemia, 12 with macroglobulinaemia, 24 with multiple myeloma, 3 with plasma cell leukaemia, and 2 with the dysgammaglobulinaemia syndrome (that is, repeated pulmonary infection with an abnormal γ-globulin electrophoretic pattern).

On the electrophoretic strip the myeloma proteins appeared in the alpha to gamma regions and the macroglobulin peaks were in the beta and gamma regions. Patients with Waldenström's purpura showed a general increase in the y-globulin peak. The C-reactive protein level was generally raised, but was often normal in patients with extensive myelomatosis involving bone. No positive results in L.E. cell tests were obtained. Positive sensitized sheep cell agglutination (the Rose-Waaler reaction) was noted in one patient with cryoglobulinaemia. 4 with Waldenström's purpura, and 6 with macroglobulinaemia. The latex and bentonite tests (using human y globulin) correlated poorly with the Rose-Waaler reaction in the patients with macroglobulinaemia. Of the 51 patients, 21 gave positive reactions in the paratoluene sulphonic acid test. The author concludes that the abnormal proteins in multiple myeloma do not show the serological reactions found in systemic lupus erythematosus and rheumatoid arthritis, but that the patients with Waldenström's purpura and macroglobulinaemia often give the positive Rose-Waaler reaction which is seen in rheumatoid arthritis.

G. L. Asherson

787. The Value of the Quinine Test for the Differentiation of Jaundice

G. K., DAIKOS, P. KOURKOUMELI-KONTOMICHALOU, and B. P. KEKIS. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 351–356, Sept., 1961. 14 refs.

The human liver contains an enzyme which metabolizes n-methyl-nicotinic acid amide. This compound has the same pyridine nucleus as quinine and quinine is therefore oxidized by a naturally occurring human liver enzyme. The present paper from the Alexandra Hospital and University School of Medicine, Athens, follows up earlier reports of the presence of this oxidase in the serum of patients with hepatocellular jaundice and its absence in cases of jaundice of a different nature. The test for its presence is performed simply. Optical density at 366 m μ is measured in a mixture of serum, buffer,

and quinine hydrochloride. The oxidized product of quinine can be recognized by its absorption at this wave length and also by its fluorescence.

A series of 120-sera were examined, 50 of them from patients with infective hepatitis. The result of the quinine oxidase test was positive in all 50 cases, but so was that of the thymol turbidity test in 49 and that of the cephalin flocculation test in 48. The result was also positive in one of 3 cases of cholangiolitis, in 8 of 9 cases of cancer of the liver, in 4 of 11 cases of cirrhosis, in all of 5 cases of gall-stones with infection of the bile canals, and in 4 of 30 cases of obstructive jaundice. In all of 5 cases of haemolytic jaundice the quinine test gave a negative result.

The authors doubt whether the results of their tests in fact indicate that there was enzymic destruction of quinine since they found an increase in the absorption at 366 m μ even if quinine was not added to the incubated mixture of serum and buffer. They consider it more likely that a positive test result reflects disturbances of protein balance in the serum of patients with hepatocellular jaundice.

H. Lehmann

MORBID ANATOMY AND CYTOLOGY

788. Exfoliated Measles Glant Cells in Nasal Secretions N. K. MOTTET and V. SZANTON. Archives of Pathology [Arch. Path.] 72, 434-437, Oct., 1961. 2 figs., 21 refs.

In an investigation at the University of Washington Medical School, Seattle, multinucleate giant cells were found in smears of nasal secretions from 36 of 52 patients with prodromal or exanthematous measles, but not in secretions from 15 patients with chicken-pox, 32 with acute coryza, and 8 with scarlet fever. The secretion was obtained from one nostril by swab, gently smeared on a glass slide, fixed in equal parts of methanol and ether, then stained by either Wright's or Papanicolaou's method. Two false positive results were attributed to clumps of degenerate epithelial cells. False negative results were presumed to be due to inadequate sampling.

A. Wynn Williams

789. Significance and Nature of Inclusion-bearing Cells in the Urine of Patients with Measles

R. P. BOLANDE. New England Journal of Medicine [New Engl. J. Med.] 265, 919-923, Nov. 9, 1961. 6 figs., 17 refs.

At the Institute of Pathology of Western Reserve University, Cleveland, Ohio, the author studied the centrifuge deposit from early-morning specimens of urine from 2 children with early eruptive measles. Smears of the deposit were stained by the Papanicolau, Feulgen, and periodic-acid-Schiff (PAS) methods and by the fluorescent anti-human-globulin technique, while aliquots of the sediment were embedded in methacrylate and sectioned for study under the electron microscope. (References to all these methods are given.) Eosinophilic inclusions, Feulgen-negative and weakly PAS-positive, were found in numerous cells. These cells measured 10 to 25 μ and the inclusion displaced the

nucleus to the side. The kidneys of 5 children who died with giant-cell reactions in the lungs or lymphoid tissues were also investigated. Three of these children had definite clinical signs of measles and the diagnosis was presumptive in the other 2, but the kidneys showed no uniform change attributable to measles and no exfoliative source of inclusion-bearing cells was demonstrated. The most striking change was hyperplasia and piling up of the epithelium of Bowman's capsule and areas of feamy cytoplasmic ballooning. In one case discrete, hyaline, eosinophilic masses were related to these altered cells, which stained positive with Lendrum's stain.

Finally, 32 children were inoculated with attenuated measles virus and their urinary sediment examined for the presence of inclusion bodies before and again 5 and 9 days after inoculation. In 9.4% of these children inclusion bodies were found before inoculation and on the 5th day, but on the 9th day 55.5% of the specimens were positive, this increase being statistically significant (P=0.002). The inclusion-bearing cells did not differ greatly from those of natural measles, but they were scantier and the inclusions were smaller, sometimes multiple, and basophilic more often than eosinophilic. Unfortunately, an epidemic of β -haemolytic streptococcal throat infection cut across the experimental period.

The author considers that the connexion between measles and urinary cellular inclusions is not proven. It may be a non-specific degenerative phenomenon. Electron microscopy of the cellular inclusions revealed a homogeneous body in contrast to the crystalline lattice of the nuclear inclusions in cells infected with measles virus. However, there is still reason to suspect a cause and-effect relation between experimental measles and cellular inclusions. One possibility is that the inclusion-bearing cells may be altered blood cells; exuded into the urine from the blood stream.

F. Hillman

790. The Tongue and Oesophagus in Iron-deficiency Anaemia and the Effect of Iron Therapy

I. McLean Baird, O. G. Dodge, F. J. Palmer, and R. J. Wawman. *Journal of Clinical Pathology [J. clin. Path.*] 14, 603-609, Nov., 1961. 5 figs., 15 refs.

A study of the correlation between the haemoglobin and serum iron levels and the clinical and histological state of the lingual and oesophageal mucosa in iron-deficiency anaemia is reported from St. Helen's Hospital, Barnsley, and the University of Sheffield. In all 14 patients studied (2 male and 12 female) the initial haemoglobin level did not exceed 10 g. per 100 ml. and the serum iron level did not exceed 50 µg. per 100 ml. Biopsy specimens of the tongue and oesophagus were taken within a week of the initial blood count and 4 weeks and 3 months after the start of iron therapy.

All 14 patients described a rapid subjective improvement. The signs of repapillation of the tongue, where atrophic, appeared after treatment for 1 to 2 weeks, and the tongue was fully papillated in 12 patients at the time the third biopsy specimen was taken. The disappearance of the angular stomatitis was much slower.

Histologically, the tongue was normal before treatment in 5 patients; in the remaining 9 the epithelium showed

no evidence of filiform papillae, and keratohyalin (eleidin) granules, normally found in compact epithelial cells deep to the papillae, were not present. With restoration of the haemoglobin and serum iron levels to normal the tongue biopsy specimens in most cases revealed the reappearance of filiform papillae and of the keratohyalin granules.

The authors failed to observe any consistent histological change in the oesophageal epithelium as seen in biopsies before or after treatment, and the relationship between postcricoid carcinoma and possible oesophageal hyperkeratinization in iron-deficiency anaemia is doubtful.

H. Caplan

791. Exfoliative Gastric Cytology: Its Evaluation in the Diagnosis of Carcinoma of the Stomach

M. F. REECE, T. H. BOON, and R. O. K. SCHADE. Lancet [Lancet] 2, 1163-1164, Nov. 25, 1961. 11 refs.

To assess the value of exfoliative gastric cytology in the early detection of carcinoma of the stomach the authors of this paper from the University of Durham and the Royal Victoria Infirmary, Newcastle upon Tyne, examined smears of gastric cells from 115 patients subsequently proved at operation or necropsy to have carcinoma of the stomach.

Carcinoma cells were found in 64% of the gastric smears, while in a further 20% atypical cells were present. The authors point out, however, that atypical cells have been found in smears from patients without gastric carcinoma. Barium-meal examination revealed a filling defect indicative of gastric carcinoma in only 47%, while in a further 27% the evidence suggested such a lesion. In a discussion the authors state that since patients with pernicious anaemia "have an increased liability to gastric carcinoma" they are observing a series of 250 such patients by examining exfoliated gastric cells every 6 months with the object of determining whether this procedure is of value in the early diagnosis of carcinoma.

J. B. Wilson

792. Retinal Vascular Patterns. IV. Diabetic Retinopathy

D. G. COGAN, D. TOUSSAINT, and T. KUWABARA. Archives of Ophthalmology [Arch. Ophthal.] 66, 366–378, Sept., 1961. 12 figs., 33 refs.

By means of a new trypsin-digest method, which makes it possible to isolate the retinal vessels and to examine the endothelial reactions in their walls, the authors have studied at the Massachusetts Eye and Ear Infirmary, Boston, the pathological changes in 55 diabetic retinae and have compared them with those seen in flat sections. and cross-sections of the retinae. Micro-aneurysms were found to occur about zones of occluded capillaries and to show a preferential loss of the mural cells. Moreover the micro-aneurysms appeared to begin at the sites of former mural cells, and the authors postulate that the loss of these cells provides a weak point in the capillary wall at which the outpouching or aneurysm occurs. Subsequently the aneurysms become hyalinized and undergo fatty degeneration and finally disintegration. Capillary dilatation was also a feature of this study,

but no intraretinal neovascularization occurs as a result of the diabetes, whereas neovascularization in the vitreous and on the inner surface of the retina does occur. The intravitreal vessels were unlike those of the normal retina, but resembled rather those seen in granulation tissue; moreover, retinitis proliferans was observed in the occasional absence of pathological changes in the retina itself, which would seem to support the idea that retinitis proliferans could be a variant rather than an end-stage of retinopathy. The haemorrhages and exudates in diabetic retinopathy consist of protein residue, fat, and cytoid bodies, but the amount of fat seen histologically was less than would have been expected from the clinical appearances.

[The findings reported in this paper are of exceptional interest.]

Norman Ashton

793. The Formal and Causal Pathogenesis of Endocardial Fibrosis in Early Childhood. (Die formale und kausale Pathogenese der frühkindlichen Endocardifibrose) G. GABLER. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie [Beitr. path. Anat.] 125, 110–122, Oct., 1961. 3 figs., bibliography.

In this paper from the Friedrich Schiller University, Jena, details are given of the anatomical and histological findings in the heart in 6 cases in which endocardial fibrosis was discovered post mortem in infants ranging in age from 5 weeks to 13 months. Congenital heart disease was present in 4 cases, membranous colitis and pulmonary atelectasis in one, and cerebral birth trauma and aspiration of amniotic fluid in the sixth. The findings suggest that this condition is due to chronic coronary insufficiency resulting in the replacement of degenerated heart muscle by fibrous tissue. A secondary increase in elastic fibres results from the changed haemodynamics.

M. Lubran

794. A Study of the Vertebral Arteries. (К исследованию позвоночных артерий)

N. V. Vereščagin. Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1304-1310, No. 9, 1961. 4 figs., 34 refs.

This paper from the Institute of Neurology, Moscow, describes an investigation by radiological, anatomical, and histological methods of the extracranial part of the vertebral arteries removed from 62 patients who had died from cerebrovascular accidents. The specimens studied consisted of the great vessels divided at their origin from the arch of the aorta, the cervical spine, and part of the occipital bone including its basilar portion: Posterior, lateral, and oblique x-ray views of the cervical spine were taken both before and after the introduction of contrast medium into the vertebral, innominate, and left subclavian arteries. The specimens were then fixed in formalin, decalcified in nitric acid, and, after examination by naked eye, embedded in celloidin. Sections 20 to 40 μ thick were prepared and stained with haematoxylin and eosin, with van Gieson's stain, and also for elastic fibres. Further sections 150 to 200 μ in thickness were also cut to study by means of a stereoscopic microscope the characteristics of the vertebral arteries in the presence of pathological changes of bone and ligament. Where radiography showed no block or narrowing the vertebral artery was studied in its whole length by laying open the foramina transversaria.

In more than half the cases there were various lesions of the vertebral artery, usually in association with lesions of the carotid arteries in the neck. The most frequent pathological finding was atherosclerosis mainly affecting the proximal part of the vertebral artery, this sometimes being present in the form of a single plaque without any sign of atherosclerosis elsewhere. In 7 cases the lumen was blocked by thrombus. In 22 cases the artery was compressed and displaced by osteophytic lipping of the articular joints of the cervical spine. The character of the changes within the arteries varied according to whether there was infarction or haemorrhage of the brain. The former was associated with pronounced narrowing or blockage, the latter with displacement of the arteries by osteophytes and only slight narrowing of their lumen. The pathological changes described in the arteries were nearly always seen in those cases showing infarction or haemorrhage in the territory of their blood supply, but rarely in the presence of pathological foci elsewhere.

G. P. McGovern

IMMUNOPATHOLOGY .

795. Rheumatold Arthritis and the Cellular Origin of Rheumatoid Factors

R. C. MELLORS, A. NOWOSLAWSKI, and L. KORNGOLD. American Journal of Pathology [Amer. J. Path.] 39, 533-546, Nov., 1961. 23 figs., 24 refs.

This work was undertaken at Cornell University Medical College, New York, in an attempt to determine the number and cellular origin of rheumatoid factors in rheumatoid arthritic synovial membrane by use of the fluorescent staining technique, employing two conjugates of different colours, namely, (1) apple-green fluorescein Isothiocynate conjugated with bovine serum albumin and its homologous rabbit antibody in the form of a soluble complex, and (2) human y globulin labelled with orange-red rhodamine B200 which was prepared by heat aggregation, these two reactants being used either simultaneously or separately or in sequence. Synovial and lymph-node tissue was obtained by biopsy from 7 adult patients with established active rheumatoid arthritis, while similar tissues from 9 patients with various joint disorders but without rheumatoid arthritis served as a

By these means rheumatoid factor was found in the cytoplasm of the plasma cells in the synovium. When the two reagents were used simultaneously some cells reacted with one, some with the other, and a few with both. Cells stained entirely by the heat-aggregated globulin reactant were more commonly seen than the other varieties. Prior treatment of the sections with aggregated globulin inhibited subsequent staining by either conjugate, while their treatment with the unlabelled immune complex inhibited subsequent staining by the labelled immune complex, but not by fluorescent aggregate. From the evidence so obtained the authors infer the existence of 2 rheumatoid factors. In lymph nodes

there was staining of the cells of the germinal centres and of plasma cells, similar in quality to that in the synovial tissue. It was noted, however, that in any particular centre the colour of staining was either all apple-green or all orange-red. These reacting factors were found to be present in all the specimens from the cases of rheumatoid arthritis, but not in the control tissues, including those showing other forms of synovitis.

G. Loewi

796. Scrological Overlap between Lupus Erythematosus, Rheumatoid Arthritis, and Thyroid Auto-immune Disease W. Hijmans, D. Doniach, I. M. Roitt, and E. J. Holborow. *British Medical Journal [Brit. med. J.]* 2, 909–914, Oct. 7, 1961. Bibliography.

In this joint study of the Middlesex Hospital Medical School, London, the Rheumatism Research Unit of the Medical Research Council, Taplow, and the University Hospital of Leiden the occurrence of a positive L.E. cell reaction, antibodies against nuclei (A.N.F.) as demonstrated by the complement fixation and fluorescent antibody techniques, a positive latex fixation reaction for the rheumatoid factor, antibodies against human liver as shown by the autoimmune complement fixation (A.I.C.F.) test, and antibodies against thyroid tissue as demonstrated by the tanned erythrocyte and other techniques has been assessed in groups of patients with systemic lupus erythematosus (S.L.E.), rheumatoid arthritis (R.A.), and autoimmune thyroid disease or combinations of these. A different control group of healthy and diseased persons was used for each test.

All the patients with S.L.E. had systemic involvement and a positive L.E. cell reaction. Patients with a clinical picture of R.A. with a positive L.E. cell reaction were not included in this group. The patients with R.A. were all "definite" or "classic" cases as defined by the American Rheumatism Association. Patients with autoimmune thyroid disease were selected because of their high tanned erythrocyte titre. Patients with S.L.E. or R.A. with evidence of thyroid disease were considered separately.

The full results are tabulated. The anti-nuclear factor reaction was positive in all but one of the 65 patients with S.L.E. studied, the A.I.C.F. reaction was positive in 37%, and the level of anti-thyroid antibody was increased in 25%. Of the 79 patients with R.A. alone, 20% had a positive L.E. cell reaction and 50% a positive anti-nuclear factor reaction. A low titre of anti-nuclear factor was found in 14 of the 182 patients with uncomplicated Hashimoto's thyroiditis. These reactions became negative if performed at 37° C. instead of room temperature. Only in 9 cases was the A.I.C.F. titre increased. In all the 7 patients with R.A. and overt thyroiditis antibodies against thyroid tissue were present, and complement-fixing antibodies to human liver were demonstrated in 5. Three of these patients had had positive L.E. cell reactions, but serum taken after prolonged cortisone therapy was negative for the antinuclear factor. In both S.L.E. and uncomplicated R.A. thyroid antibodies occurred only in women. On the other hand the A.I.C.F., latex fixation, and anti-nuclear

factor reactions were positive in equal numbers in the 2 sexes. This suggests that the thyroid antibody may be related to a thyroid abnormality which is commoner in women than men rather than to a general abnormality of the antibody-producing system.

Discussing their findings, the authors suggest that autoimmune disease can be divided into two groups. In "disturbed antigen" disease it is considered that antigen. which fails to reach the antibody-producing system during the critical time for the induction of immunological tolerance, escapes from the tissues and provokes an immune response from a relatively normal antibodyproducing system. On the other hand in "disturbed tolerance" disease the immune response occurs against widely distributed antigens to which the normal subject is presumably tolerant. Here a primary abnormality of the antibody-producing system is postulated. In Hashimoto's thyroiditis the increased familial incidence of various thyroid disorders, including thyrotoxicosis, suggests a primary abnormality of the thyroid gland, while in S.L.E. the familial incidence of hypergammaglobulinaemia suggests a primary abnormality of the antibodyproducing system. The antibodies occurring in these diseases may be considered in 3 groups—the organspecific antibodies (such as those against thyroid tissue), the A.I.C.F. antibody, which reacts with non-organspecific cytoplasmic antigens, and the antibodies against nuclei. These anti-nuclear antibodies occur in nearly all cases of S.L.E., many cases of Sjögren's disease, and some cases of R.A. and hepatitis. The authors suggest that they may provide an index of disturbed immunological tolerance. G. L. Asherson

797. A Stable Sheep Cell Preparation for Detecting Thyroglobulin Auto-antibodies and its Clinical Applications A. J. Fulthorpe, I. M. Roitt, D. Doniach, and K. Couchman. *Journal of Clinical Pathology [J. clin. Path.*] 14, 654–660, Nov., 1961. 3 figs., 25 refs.

The preparation of fresh tanned erythrocytes is time-consuming and therefore often inconvenient. In this paper from the Wellcome Research Laboratory, Beckenham, and the Middlesex Hospital Medical School, London, the authors describe a stable preparation of thyroglobulin-coated erythrocytes which can conveniently be used for detecting autoantibodies in the serum of patients with thyroiditis. Briefly, sheep erythrocytes are treated with tannic acid, coated with human thyroglobulin, and then treated with formalin. The preparation is stored at 4° C., is available for use at any time, and is stable for at least 9 months.

Agglutinin titres obtained with this preparation were fairly well correlated with the absolute levels of serum antibody estimated by quantitative techniques. A better correlation with absolute values could be achieved by the use of a haemagglutination inhibition test in which constant amounts of thyroglobulin were added to serum dilutions before they were titrated against thyroglobulin-treated cells. The application of this and other immunological tests to the differential diagnosis of thyroiditis, thyroid cancer, non-toxic nodular goitre, primary myxoedema, and thyrotoxicosis is discussed.

M. C. Berenbaum

Microbiology and Parasitology

798. Comparison of the Resistance of the Intestinal Tract to Poliomyelitis Virus (Sabin's Strains) in Persons after Naturally and Experimentally Acquired Immunity. [In English]

Y. S. GHENDON and I. I. SANAKOYEVA. Acta virologica [Acta virol. (Bratislava)] 5, 265-273, Sept., 1961. 14 refs.

The authors, working at the Scientific Research Institute of Virus Preparations and the Municipal Orthopaedic Hospital, Moscow, compared the resistance of the alimentary tract in groups of subjects with differing states of immunity to polioviruses by challenging them with 106 TCD₅₀ of Sabin's attenuated poliovirus Type 1 by mouth. The first group consisted of 30 children aged 1 to 3 years without detectable antibody to any of the poliovirus types. Of these, 24 excreted virus for periods of 7 to 24 or more days (mean 20.4 days) in high titre and all 24 developed circulating antibody to the virus. No cytopathic virus was detected in the faeces of the 6 uninfected children. All but one of the strains of excreted virus possessed unchanged genetic markers; one strain possessed markers resembling those of a virulent strain.

The second group, consisting of subjects with naturally acquired immunity, was composed of 3 subgroups. The first consisted of 32 children aged 1 to 3 years whose sera contained a high titre of antibody to all three types of poliovirus, the second of 12 children aged 7 to 15 years and 6 adults who had recovered from paralytic poliomyelitis several years previously, and the third of 19 healthy children who had excreted poliovirus Type 1 for 4 weeks but who had ceased to excrete virus 2 months before being challenged. Virus was excreted by approximately 35% of both the first and third subgroups, but compared with the non-immune group both the amount and duration of excretion were reduced. None of the 18 individuals recovered from paralytic poliomyelitis excreted the challenge virus, but when challenged with Sabin's strain of Type-2 poliovirus in similar dosage one month later 5 were observed to excrete this strain for 3 to 5 days in low titre. In all 3 subgroups antibody levels were relatively unaltered and no change was found in the genetic markers of the excreted virus.

The third group consisted of 2 subgroups with artificially acquired immunity. The first contained 31 children aged 1 to 3 years who had received 2 injections of Salk's vaccine and the second 33 children aged 1 to 3 years who had been vaccinated with Sabin's living attenuated oral vaccine. Antibodies were present after, but not before vaccination. Of the Salk-vaccinated subgroup, 74% excreted virus in relatively high titre, although 10 times less than in the non-immune group, while the duration of excretion was reduced by one-half (mean 12·3 days). Of the Sabin-vaccinated subgroup, 37% excreted virus for a shorter period (mean 4·6 days) and in reduced amount. No rise in serum antibody

titre was observed in the Sabin-vaccinated subgroup, whereas a rise was detected in some members of the Salk-vaccinated subgroup.

A group of 32 children who had been vaccinated with monovalent Sabin vaccines of the three different policivirus types at intervals of 4 weeks, were followed up and found to excrete virus of Types 2 and 3 4 to 5 months later. Some of these strains possessed genetic markers resembling those of virulent strains. The authors succeeded in demonstrating that faecal antibody made a transient appearance in a small proportion of the Sabin-vaccinated children when challenged with Type-1 virus.

J. E. M. Whitehead

799. Antibody in Hepatitis Patients against a Newly Isolated Virus

J. P. O'MALLEY, H. M. MEYER JR., and J. E. SMADEL. Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol. (N.Y.)] 108, 200-205, Oct. [received Dec.], 1961. 2 figs., 13 refs.

In an investigation at the National Institutes of Health, Bethesda, U.S.A., a cytopathogenic virus was isolated in primary rabbit kidney culture from a plasma pool derived from patients with serum hepatitis. The infectivity of the plasma had been demonstrated in earlier volunteer studies by other workers and the plasma had been stored dried since 1951.

The virus was serially transmissible in rabbit kidney and in chick embryo cultures. Cytopathic changes appeared at the 4th to 6th days of incubation and rapidly progressed to complete cellular degeneration. The virus also grew in a variety of human and animal primary cell cultures and stable cell lines. A plaque-reduction neutralization test in chick embryo monolayer cultures was used for serum antibody titrations. Laboratory procedures and the composition of the modified 199 plaque medium with agar used are described.

The virus failed to produce clinical disease or gross lesions in 8 species of laboratory animal or in embryonated eggs; in the latter, however, blind passage established that inapparent infection had occurred.

Attempts to produce haemagglutination with the virus were unsuccessful. The physical properties of the virus are described.

Neutralization tests were negative with normal sera of 6 animal species and with antisera against a number of recognized human viruses. Neutralizing antibodies, except in low titre in some guinea-pigs, were not detectable after inoculation of the virus into laboratory animals.

The virus was not neutralized by any of 400 serum samples from registered blood donors or from 20 samples of human γ -globulin samples.

Neutralizing antibodies against the virus were titrated in sera from 30 volunteers who, in an earlier investigation by other workers, had developed serum hepatitis after the injection of (a) plasma from the pool from which the present virus was isolated, (b) 4 further icterogenic plasma samples, or (c) infected human thrombin. All except 2 of the volunteers showed a 4-fold (or greater) rise in antibody titre in late sera (taken 3 to 30 weeks after injection) as compared with early sera (taken before injection from 16 volunteers and 1 to 3 weeks after injection from 14).

In addition, 4 groups of cases of infective hepatitis were examined serologically. Neutralizing antibodies were present in serum dilution of 1:10 or more in (a) 2 of 12 cases occurring in the U.S.A. and (b) 9 of 128 cases occurring after a visit to Italy; but were not detectable in (c) 24 cases occurring in Korea and (d) 3 cases among children in New York. In no instance, where paired sera were available, was a significant rise in antibody titre observed.

[The isolation in tissue culture of viruses from hepatitis cases is being energetically pursued at the present time in the U.S.A. (and in Russia (see Abstract 802)). For a useful summary of recent developments, see Lancet, 1961, 2, 1297.]

Joyce Wright

800. Virological Studies on Acute Respiratory Disease in Young Adults. 1. Isolation of ECHO 28

D. Hamre and J. J. Procknow. Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol. (N.Y.)] 107, 770-773, Aug.-Sept. [received Nov.], 1961. 13 refs.

The JH and 2060 viruses, which are associated with mild acute respiratory disease, have been shown to be antigenically similar and have been designated E.C.H.O. 28 by the Committee on E.C.H.O. Viruses (Pelon, Amer. J. Hyg., 1961, 73, 36). Isolation of 8 further strains of E.C.H.O. 28 virus by workers at the University of Chicago is here reported.

A virological study of naturally occurring acute respiratory disease was carried out on 101 volunteer medical students aged 20 to 31 years. Nose and throat swabs were taken from them regularly at 6-week intervals throughout one academic year and also at the onset of any acute respiratory illness; the specimens were examined for viruses by tissue-culture methods. One virus (unidentified) was isolated from asymptomatic students at the routine swabbing. During October, 1960, 49. students developed acute respiratory illness, usually mild coryza with sore throat. They yielded 14 viruses in human kidney culture alone or in both human and monkey kidney culture. Of the 14 viruses, 8 were identified as E.C.H.O. 28 in neutralization tests with guinea-pig antiserum prepared with JH virus. One of these strains was selected as a prototype and designated 3/Chicago/60. Cross-neutralization tests with guinea-pig antisera revealed no significant antigenic differences between JH, 2060, and 3/Chicago/60. The remaining 6 viruses isolated from students with respiratory illness were unidentified and are being further studied. A 4-fold or greater rise in neutralizing antibody titres between acute and convalescent sera and the 3 E.C.H.O. 28 virus strains (JH, 2060, and 3/Chicago/60) was found in 7 of the 8 students from whom E.C.H.O. 28 had been isolated. Titres to the 3 strains were very similar. A rise

in E.C.H.O. 28 virus neutralizing antibody titre was not found in any of the other 49 students with respiratory illness.

Details of laboratory procedures are given. Reduced bicarbonate content (0 03%) of maintenance media and lowered incubation temperature (33° C.) of tissue cultures were used, as in the work by Tyrrell et al. (Lancet, 1960, 1, 235; Abstr. Wld Med., 1960, 28, 95) on common cold viruses.

Joyce Wright

801. A New Virus Group Designated R-Virus. (Грунпа штаммов нового вируса, навванного Р-вирус) R. S. Dreizin, V. E. Javorovskaja, A. M. Balandina, S. P. Šurin, N. N. Vorob'eva, A. N. Mosolov, G. D. Zalesskij, and V. M. Ždanov. Вопросы Вирусоловии [Vop. Virusol.] 6, 521–532, Sept.—Oct., 1961. 4 figs., 12 refs.

During the period 1956-60 a total of 57 strains of a new group of viruses were isolated at the Medical Institute, Novosibirsk, from blood, mouth washings, faeces, and biopsies from the atrial appendages of patients with rheumatic fever and 4 strains were isolated post mortem from the heart, kidney, and spleen. These strains have now been investigated in greater detail in collaboration with the Ivanovski Institute for Virology, Academy of Medical Sciences, Moscow, with the following results.

The size of the virus as determined by electron microscopical measurements is 150 to 180 m μ . The virus passes through Seitz filters and 99% of the virus particles are deposited in the ultracentrifugal sediment after 14 hours at 36,000 g. The virus multiplies rapidly in cultures of human foetal fibroblasts with marked cell degeneration. It does not multiply and causes no cell degeneration in tissue cultures of rhesus monkey kidney and causes only partial degeneration in tissue cultures of human epithelium such as KB, Hep-2, HeLa, and SOZ. The morphological changes seen in human fibroblast cultures are the formation of large, round, basophilic cells which quickly degenerate, forming pyknotic nuclei. R virus is not pathogenic for adult and suckling white mice, guinea-pigs, rabbits inoculated intracerebrally or intracorneally, or chick embryos. However, when inoculated paratracheally some strains of R virus may cause carditis in rabbits. Intravenous inoculation leads only rarely to carditis. R virus is not killed by exposure to 20% ether for 12 to 18 hours at 4° C., but is killed by 5% phenol solution. It survives quick freezing at -70° C. and thawing to 37° C., keeps for 3 months and longer at -20° C., is slowly inactivated during the course of a month at room temperature and at 36° C., and is completely inactivated when kept at 70° C. for 10 minutes.

Antigenically, 14 strains investigated were homologous. No antigenic relationship could be shown with strains of E.C.H.O. viruses 1 to 20, Coxsackie virus A9 and B1 to 5, adenovirus 1 to 7, herpes virus strains K and P2, or human erythrocytes Group O. The erythrocytes of fowl, guinea-pigs, rhesus monkeys, and white mice were not agglutinated at 37° C. or 4° C. In a few convalescent sera neutralizing antibody titres of 1 in 5 and 1 in 10, and rarely of 1 in 20, were found. K. Zinnemann

802. The Isolation of Virus Strains in Infective Hepatitis. (О выделении штаммов вируса при эпидемическом гелатите)

V. A. Anan'ev and A. K. Šubladze. Bonpocu Bupyconoeuu [Vop. Virusol.] 6, 538-542, Sept.-Oct., 1961. 1 fig., 6 refs.

The first successful cultivation of human kidney tissue from stillbirths was used at the Ivanovski Institute for Virology, Academy of Medical Sciences, Moscow, for the isolation of virus strains from the faeces of patients during the first days of an attack of infective hepatitis. From 20 faecal-specimens from early cases 5 strains were isolated, while from 40 specimens taken at later stages only one virus strain could be isolated. In kidney tissue culture cell degeneration developed on the 3rd to 4th day from the first passage onwards and consisted in round-cell accumulations which, on the 5th to 6th day, came off the glass wall of the container. On further passaging degeneration had already started after 24 to 48 hours. With all strains isolated attempts were made to infect tissue cultures of monkey kidney, kidney from the dog, calf, and guinea-pig, tissue culture lines from human tissues, such as KB, HeLa, Hep-1, Hep-2, amnion cells, tonsillar tissue, lymph nodes, and fibroblasts, and chick embryos. Apart from human kidney culture lines only HeLa and Hep-2 cell cultures and chick embryos were able to support growth of the new

The strains isolated from the faeces in cases of human infective hepatitis were compared with other viruses such as poliovirus, Coxsackie virus, E.C.H.O. viruses, adenoviruses, herpes virus, and the virus of infective hepatitis of the dog. The human hepatitis strains could be distinguished from other human enteroviruses by the fact that they would not grow in monkey kidney tissue cultures. Antisera to the other enteroviruses did not neutralize the cytopathogenic effect of the new virus strains even in as low a concentration as 10 minimal cytopathogenic doses, while homologous antisera easily neutralized 100 doses. Paired sera from patients convalescent from hepatitis showed no neutralizing titres in the first sample and titres varying from 1 in 32 to 1 in 128 in the second sample. In one case no neutralizing antibody was demonstrated in either sample.

Hepatitis strain K3 was more completely investigated. It passed through Seitz filters and was non-pathogenic for fully grown and newborn mice, guinea-pigs, rabbits, and dogs. In dogs a small rise of temperature was noticed after infection, without any clinical symptoms. When subsequently inoculated with the Karabash strain of canine hepatitis the animals developed the full clinical symptoms of the disease. Thus there was no cross-immunity. The virus was resistant to the action of bile and ether for 72 hours and withstood heating to 50° C. for 10 minutes. None of the strains isolated agglutinated human or monkey erythrocytes, but in low dilutions haemagglutination of fowl erythrocytes was observed. Antigens prepared from culture fluid containing virus particles gave no complement fixation with specific adenovirus antiserum.

Thus it appears that the biological, cultural, and antigenic properties of the newly isolated viruses allow them to be regarded as an entity apart from the hitherto known enteroviruses. Their presumptive aetiological role in infective hepatitis of man, however, can be ascertained only by further comparative studies of the large and complex group of viruses which can be isolated from human facces.

K. Zinnemann

803. The Nature of Penicillin Resistance in Staphylo-cocci

R. KNOX and J. T. SMITH. Lancet [Lancet] 2, 520-522, Sept. 2, 1961. 17 refs.

In laboratory studies at Guy's Hospital Medical School, London, it was found that naturally occurring variants of Staphylococcus pyogenes which were resistant to methicillin and also strains which had become resistant as a result of "training" by growth in gradually increasing concentrations of the antibiotic were also resistant to the other penicillins tested—benzylpenicillin, phenoxymethylpenicillin, phenoxymethylpenicillin, phenoxythylpenicillin, phenoxypropylpenicillin, and a new penicillin ampicillin ("penbritin"; BRL 1341). This resistance was found to be an intrinsic or inherent characteristic of the strains and independent of their ability to form penicillinase.

It was also found that a strain of this organism, naturally resistant to methicillin and to the other penicillins enumerated above, might become so resistant as a result of further subculture in methicillin that it would survive exposure to $1,000 \mu g$. per ml., but that its ability to resist the other penicillins was not increased.

R. Hare

804. Further Investigation on the Usefulness of the Direct Qualitative Micro-niacin Test for Distinguishing Human Tubercle Bacilli from Other Mycobacteria. A Comparative Study of Technics Using Fresh and Stored Cultures of Varying Ages

M. S. TARSHIS. Diseases of the Chest [Dis. Chest] 40, 374-380, Oct., 1961. 10 refs.

The author has recently described three micro methods for the semi-quantitative detection of niacin in cultures of mycobacteria. These depend on the use of cyanogen bromide with aniline, benzidine, and orthotolidine. In the present paper from the Veterans Administration Hospital, Alexandria, Louisiana, he describes a comparative study of the efficacy of these methods in detecting niacin production in fresh and stored strains of human, bovine, and avian Mycobacterium tuberculosis, and saprophytic and "unclassified" mycobacteria. In fresh cultures all the human-type tubercle bacilli gave slightly to intensely positive results, whereas all the other strains, with two exceptions, gave negative or doubtful results. After 7 to 10 days the results of the tests with aniline and benzidine were slightly better than those with orthotolidine. Similar results were obtained with stored cultures, but the sensitivity of the tests was virtually the

The author states that in most instances the results given by human tubercle bacilli are sufficiently distinct to permit identification, but recommends that other tests should be employed in conjunction with the niacin test for greater effectiveness.

John M. Talbot

Pharmacology and Therapeutics

805. Treatment of the Hyperthermic Syndrome with Chlorpromazine. (К лечению гипертемического синдрома хлорпромавином (аминазином))

B. Raška. Педиатрия [Pediatrija] 40, 43-46, Nov., 1961. 11 refs.

Previous experimental studies by the author and colleagues at the Charles University, Prague, on rabbits subjected to overheating had shown that chlorpromazine and also acetylpromazine were effective in preventing death from hyperthermia in 60% of cases. More recently the author has shown that these drugs also prevent ventricular fibrillation induced by injections of potassium chloride. A raised serum potassium level has been found in hyperthermia.

As a result of his experience with chlorpromazine in the treatment of 94 children with hyperpyrexia, including . 17 with the hyperthermic syndrome and the remainder with bronchopneumonia, encephalitis, and other diseases, he advises the following regimen. (1) At the earliest possible moment chlorpromazine should be given by intravenous injection in a dosage of 1 to 3 mg. per kg. body weight every 24 hours while the hyperthermia. continues. The infusion must be given slowly, not more than 1 mg. per kg. being administered per minute. (2) This should be followed by an intravenous drip of 5% glucose, with or without 1/5 N saline solution. Poluch has given this at a temperature of 3° to 5° C. but the present author recommends cold packs in the form of ice-bags to the groins, praecordium, and carotid arteries in the neck, or even immersion of the whole body in cold water for a few minutes at a time. (3) Aspiration of the stomach contents. (4) If convulsions persist the dose of chlorpromazine should be repeated, if necessary with the addition of promethazine in the same dosage or phenobarbitone, 10 to 20 mg. per kg. in 24 hours. (5) Antibiotics should be given as required for the basic disease, while asphyxia or cyanosis is an indication for nursing in an oxygen tent.

The mortality in the author's series of 94 cases was 14.8%, which is only one-fifth of that reported by Rössler and Polacek in 1954.

L. Firman-Edwards

806. Experimental Study of the Effects of Persantin on the Coronary Circulation and Myocardial Metabolism under Basal Conditions. (Étude expérimentale des effets de la persantine sur la circulation coronarienne et le métabolisme myocardique dans les conditions basales) D. LAURENT, J. L. CHEVRIER, and M. MOUQUIN. Presse médicale [Presse méd.] 69, 2292-2294, Nov. 25, 1961. 3 figs., 23 refs.

The pharmacodynamic action of "persantin" [2:6-bis-(diethanolamino)-4:8-dipiperidinopyrimido-(5:4-D)-pyrimidine] on myocardial metabolism under conditions in which the heart has been excluded from the circulation has been studied in dogs at the Hôpital Broussais, Paris.

The experimental technique for measuring the coronary blood flow was similar to that used by Lenfant et al. (Sem. Hôp. Paris, 1957, 5, 2195). Persantin (0.3 to 1.0 mg. per kg. body weight) was administered by intraarterial injection or continuous infusion (0.02% in physiological saline) to 6 prepared dogs and the variations in coronary flow followed for one hour. Persantin showed two distinct effects, vasodilator and metabolic. The coronary vasodilator effect was irregular and was probably caused by the special conditions of the experiment. The normal effect of persantin is on the myocardial metabolism of oxygen; this was shown by an increase in the oxygen level and a decrease in that of carbon dioxide in the venous outflow of the coronary J. E. Page circulation.

807. Some Pharmacological Properties of a New Intramuscular Iron Preparation

P. O. SVÄRD. Journal of Pharmacy and Pharmacology [J. Pharm. Pharmacol.] 13, 641-649, Nov., 1961. 4 figs., 11 refs.

The pharmacological properties of an iron-sorbitolcitrate complex (" jectofer") containing 50 mg. of iron per ml. were investigated at a pharmaceutical laboratory in Sweden in cats, rabbits; rats, mice, and guinea-pigs. The rapid intravenous injection of doses of jectofer containing 2 to 10 mg. of Fe per kg. body weight in cats and rabbits caused a transient fall in blood pressure. The preparation was less potent than ferrous sulphate, but more potent than iron-dextrose in this respect. On making repeated intravenous injections tachyphylaxis developed. The fall in blood pressure was not influenced by atropine or antihistaminic drugs, but it did not occur if the iron-sorbitol was injected slowly. In cats the local injection of iron-sorbitol (60 mg. Fe per kg.) or iron-dextran into the femoral artery did not increase the peripheral resistance. Since ferric chloride precipitates when mixed with blood and does increase the peripheral resistance when injected locally into the femoral artery, it was concluded that iron-sorbitol does not precipitate in the blood vessels.

In rabbits intravenous doses of iron-sorbitol of less than 100 mg. Fe per kg. body weight did not affect the respiration, but higher doses produced periods of apnoea. Cats' required doses in excess of 170 mg. Fe per kg. to influence respiration. The normal electroencephalographic pattern was not influenced unless lethal doses were given. When the drug was administered by the intravenous and subcutaneous routes to mice and rabbits its LD₅₀ was between 35 and 38 mg. Fe per kg.; given by the intramuscular route in rats the LD₅₀ was 48 mg. Fe per kg. In subchronic toxicity tests in rabbits 25 animals were given a total of 215 mg. Fe per kg. during 9 weeks: During this test 3 animals died, all having had diarrhoea before death; one of these was from the

control group. Post-mortem examination was negative except for signs of enteritis. In a second group, receiving a total dose of 110 mg. Fe per kg., no animals died as a result of the iron injections. The haemoglobin concentrations, haematocrit values, and erythrocyte counts were not consistently affected, and there was no significant proteinuria. Post mortem the distribution of iron did not differ essentially from that previously described for iron-dextran. The preparation did not have antigenic properties, nor were there any signs of anaphylaxis in sensitized guinea-pigs.

P. A. Nasmyth

808. Mechanism of Absorption of Two Intramuscular Iron Preparations

P. O. SVÄRD and S. LINDVALL. Journal of Pharmacy and Pharmacology [J. Pharm. Pharmacol.] 13, 650-653, Nov., 1961. 2 figs., 3 refs.

In this further study [see Abstract 807] the absorption of the iron-sorbitol preparation "jectofer" was compared with that of iron-dextran ("imferon") in cats anaesthetized with pentobarbitone sodium. Each preparation contained the same amount of elementary iron per unit volume and was administered in a dosage corresponding to 3 mg. Fe per kg. body weight by deep injection into the gluteal region, the leg being exercised mechanically throughout the observation period. Lymph was collected continuously from the thoracic duct and samples of arterial blood were taken 6 to 8-times at 15-minute intervals during a 2-hour period.

It was found that the serum iron level rose more rapidly after the injection of iron-sorbitol than after that of iron-dextran, and that tying the lymph vessels from the injected region slowed the rate of rise of the serum iron concentration; thus part of the dose was absorbed directly into the blood stream. In experiments in which lymph was continually collected by cannula from the thoracic duct and prevented from entering the blood, the serum iron level rose after the injection of ironsorbitol with a simultaneous decrease in unsaturatediron-binding capacity, but these changes were not observed when iron-dextran was injected. In the same experiments both preparations caused a rapid rise in the iron content of the lymph, but the onset of absorption was usually more delayed with iron-dextran. Once absorption of the latter into the lymph was established however it proceeded at the same rate as absorption of iron-sorbitol. The predominant importance of molecular size in the absorption of a compound is discussed. It was calculated that 50 to 60% of the injected dose of iron-sorbitol was absorbed by the blood in the 2-hour experimental period. P. A. Nasmyth

809. Comparison of Effects of Protamine and Polybrene, with Special Emphasis on the Factor VIII (Antihemophilic Globulin) Deficiency Induced

H. A. Perkins, G. Harkins, F. Gerbode, M. R. Rolfs, and D. J. Acra. *Journal of Clinical Investigation [J. clin. Invest.*] 40, 1421–1430, Aug., 1961. 8 figs., 24 refs.

The authors describe an experimental study on dogs of the comparative effects of the heparin antagonists protamine and "polybrene" (hexadimethrine bromide), which was carried out at the Presbyterian Medical Center, San Francisco, with the aim of determining which of the two gave the better results. The drugs were given by intravenous injection in doses of 5 mg. per kg. body weight.

Both drugs showed a similar tendency to produce profound hypotension, accompanied by tachycardia followed by bradycardia and slowing of the respiration with subsequent tachypnoea. Weight for weight, polybrene was a more powerful antagonist of heparin than protamine; it tended, however, to produce greater disturbance of blood clotting. Both substances disappeared very rapidly from the blood; as judged by a heparin titration technique there was frequently none detectable 10 minutes after the injection. A second injection of either drug disappeared much more slowly however, suggesting that the mechanism for removing the drug had temporarily reached saturation. The addition of protamine or polybrene to blood in vitro is known to produce an interference with thromboplastin generation. In vivo, however, a specific depression of antihaemophilic globulin concentration was surprisingly found to be accompanied by a rise in the concentration of Factor V. This depressed concentration of antihaemophilic globulin persisted for at least one hour-much longer than did the measurable level of polybrene or protamine in the circulation. Both these heparin antagonists also produced a depression of the platelet count, but this usually had returned to normal with one hour.

Pointing out the practical significance of these findings the authors note that in cardiac surgery involving an extracorporeal circulation there is a tendency, should bleeding continue, for the surgeon to demand more polybrene than is required to neutralize the heparin, but this study shows that such additional polybrene may aggravate the haemorrhage. In general the effects of the two compounds were so similar that the authors found little reason to prefer one over the other.

[This is a very valuable contribution.]

A. S. Douglas

810. The Cardiovascular Actions of Suxamethonium in the Cat

C. M. Conway. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 560-564, Nov., 1961. 4 figs., 14 refs.

The cardiovascular actions of suxamethonium were studied in 12 spinal cats and 4 cats with intact central nervous systems. Suxamethonium in doses of 0.5 to 10 mg. per kg. caused an initial transient fall in blood pressure followed by a more sustained rise in pressure in both spinal and intact cats. In spinal cats there were no alterations in heart rate; in intact cats there was a moderate tachycardia which could be abolished by vagal section. The fall in pressure could be prevented by atropine and the rise in pressure could be abolished by hexamethonium. Doses of suxamethonium greater than 10 mg. per kg. caused a more marked rise in blood pressure accompanied by a marked tachycardia. This effect of larger doses of suxamethonium did not occur in animals treated with reserpine.

The significance of these findings is discussed.—
[Author's summary.]

Infectious Diseases

811. Investigations of Toxoplasmosis in Czechoslovakia. (Исследование токсоплавмоза в Чехословании)
О. Іпочес. Педиатрия [Pediatrija] 40, 24—29, Nov., 1961.

The first case of congenital toxoplasmosis to be recognized as such was described by the ophthalmologist Yanku in 1923 and preparations from this case were studied by Leviditi in 1928. Since then several further cases have been reported. In modern times the diagnosis is based on four tests: (1) the Sabin-Feldman dye test, which is very reliable but complex in technique and is only possible in-well equipped laboratories; (2) the complement fixation reaction; (3) Fraenkel's intradermal test; and (4) the haemagglutination reaction, in the testing stage.

In the present investigation, carried out over a wide area of Czechoslovakia (chiefly rural), of 4,000 persons of all ages subjected to tests 700 gave a strongly positive response to the intradermal test and 360 a weakly positive response. The percentage of positive results rose with age; thus only 4.6% of the 172 children aged under 5 years gave a positive reaction, whereas of 195 persons over 70 years of age 55% did so. The problem of infantile and congenital toxoplasmosis is therefore only a small part of a much larger one. But the percentage of positive reactors among mothers of children with congenital deformities and mental defects was much higher than in mothers of normal children (60 to 70% compared with a normal average at the childbearing age of 20 to 30%). The mean figure for the fathers of these abnormal children was 25 6%. The highest proportions of positive reactions were found in cases of choroidoretinitis (71.4 to 88%) and in patients with Buerger's disease (70%), while in patients with thrombophlebitis it was 67%. It is suggested that toxoplasmosis may be an aetiological factor in several diseases, at any rate in Czechoslovakia.

An investigation of mammalian fauna by a number of observers revealed a considerable degree of infection by Toxoplasma. Rabbits, goats, cats, chamois, and dogs (in that order) all showed high incidences (79, 72, 66, 50, and 42% respectively). Rats, horses, and pigs were surprisingly, much less infected, while cattle and sheep occupied an intermediate position. There is thus a large animal pool from which infection to human beings could be transmitted.

L. Firman-Edwards

812. Association of Coxsackie Viruses with Illnesses Resembling Mild Paralytic Poliomyelitis

R. L. MAGOFFIN, E. H. LENNETTE, and N. J. SCHMIDT. *Pediatrics [Pediatrics]* 28, 602-613, Oct., 1961. 22 refs.

Virological studies were undertaken at the State Department of Public Health during 1955 to 1957 on all suspected cases of poliomyelitis throughout the State of California. Of 713 cases diagnosed as non-paralytic

poliomyelitis or aseptic meningitis the stools yielded poliovirus in 60 (8%), Coxsackie virus in 157 (22%), and E.C.H.O. or unidentified enteric viruses in 66 (9%); no cytopathogenic organism was detected in the remaining 430 cases. Stools from 497 cases diagnosed as paralytic poliomyelitis yielded polioviruses in 267 (54%), E.C.H.O. 6 virus in 3 cases, unidentified viruses with E.C.H.O. characteristics in 12 cases, and Coxsackie virus in 25 (5%); the type of Coxsackie virus isolated was A9 in 3 cases, B2 in 6, B3 in one, B4 in 8, B5 in 6, and both B4 and B5 in one.

This paper relates to the 25 cases with a clinical diagnosis of paralytic poliomyelitis and shown to have a Coxsackie virus infection. Clinical and laboratory findings for each case are tabulated. Serological tests, which were performed in 16 cases, made it unlikely that polioviruses were related to the illness, and the laboratory diagnosis of Coxsackie virus infection was supported by significant rises in titre (4 cases) or raised titres (1:32 or more in 10 cases) of homotypic neutralizing antibody. Of these 22 male and 3 female patients only 3, aged 16, 37, and 64 years respectively, were over 12 years of age. Initially the clinical manifestations were those of benign' aseptic meningitis. Muscle weakness appeared during, the first week of illness and was mild in 20 cases, moderate in 4, and severe in one, in a man aged 64. The involvement was usually asymmetrical and limited to a few muscle groups, with some predilection for the girdle musculature. There were no clinical differences relatable to a particular Coxsackie virus type. It is suggested that mild to moderate paresis in Coxsackie virus infections fills the gap in the clinical spectrum between benign aseptic meningitis and infrequent severe paralysis. The literature relating to Coxsackie infection and central nervous system involvement is reviewed.

Joyce Wright

813. Para-Influenza 2 (CA) Virus: Etiologic Association with Croup

H. W. Kim, A. J. VARGOSKO, R. M. CHANOCK, and R. H. PARROTT. *Pediatrics* [*Pediatrics*] 28, 614–621, Oct., 1961. 10 refs.

The role of para-influenza-2 (croup-associated) virus in acute respiratory illness of children was investigated during October to December, 1959, at the Children's Hospital of the District of Columbia, three categories of patient being studied: (1) those with the croup syndrome, (2) those with other respiratory tract illness, and (3) those with no respiratory tract disease, these being matched for age with the other two groups. Virus isolations were made from oropharyngeal swabs in monkey kidney cultures, which were then examined for cytopathic changes and tested for haemadsorption. Isolates were identified by haemadsorption-inhibition, using specific rabbit antisera. Evidence of infection depended upon virus isolation or a 4-fold rise in complement-fixing

antibody titre during illness, or both. Routine bacteriological examinations yielded no significant results among the patients with croup.

Evidence of para-influenza virus infection was foundin 20 (71%) of the 28 cases of croup, this being of Type 1 in 7 cases (25%), Type 2 in 10 (36%), and Type 3 in 3 (11%). Isolation of virus was successful in 16 (57%) of the cases. A tabulated analysis of para-influenza 2 virus isolations arranged according to case-category, race, geographical home area, and socio-ecónomic status is given. Para-influenza 2 virus was isolated from 7 of the 28 croup cases, only one of 267 cases of other respiratory tract illness, and only one of 203 patients without respiratory tract illness. All 7 isolations from croup cases were derived from 24 private patients, most of whom were drawn from two geographic home areas. Clinical features of the croup cases are described and detailed in a table. Most of them were severe. Cases with para-influenza 2 virus were clinically indistinguishable from those with virus of Types 1 or 3.

An analysis of 143 cases of croup seen during 1957-60 showed that an association with myxovirus infection was present in 52% (influenza virus in 8%), para-influenza virus Type 1 in 26%, Type 2 in 8%, and Type 3 in 10%. The possibility of including para-influenza viruses in a vaccine against respiratory tract infection in young children is discussed.

An addendum contains data obtained after completion of the 1959 study, when 1,664 oropharyngeal swabs from children with respiratory tract illnesses were examined and 829 from control patients. Para-influenza 2 virus was isolated from 12 children only, all of whom had lower respiratory tract illness (bronchiolitis and bronchopneumonia in one case each, and bronchitis and pharyngitis in 10), but none of whom had croup. Thus, although the virus was again associated with respiratory tract illness, the different distribution according to diagnosis in this series and that of 1959 could not be explained.

Joyce Wright

814. Eaton Agent Pneumonia—Clinical Features

M. A. MUFSON, M. A. MANKO, J. R. KINOSTON, and R. M. CHANOCK. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 369–374, Oct. 28, 1961. 5 figs., 13 refs.

A high incidence of infection due to Eaton agent among military recruits with respiratory illness at Marine Corps Recruit Depot, Parris Island, South Carolina, provided an opportunity to study by epidemiological and clinical methods a large number of serologically proved cases of Eaton-agent pneumonia.

The symptoms and signs in 109 cases of Eaton-agent pneumonia, 23 cases of adenovirus pneumonia, and 122 cases of aetiologically undiagnosed atypical pneumonia were recorded. The course of the illness in untreated patients with Eaton-agent pneumonia (50), adenovirus pneumonia (15), and aetiologically undiagnosed pneumonia (59) was also noted. Serological identification of Eaton-agent pneumonia was determined by demonstrating specific fluorescent stainable antibody to Eaton agent during convalescence.

In Eaton-agent pneumonia an abrupt onset of illness was followed by a short period of fever, cough, chills, headache, malaise, and fatigue. Rales were noted in 84% of cases. Radiologically, unilateral involvement of the lower lobes was the most frequent finding, bilateral involvement being noted in 19% of cases. In most cases the symptoms subsided in 3 to 10 days and the chest signs and radiological abnormalities cleared in 7 to 21 days; in one-quarter of the patients, however, symptoms were still present after 4 weeks. Cold agglutinins developed in 49 (45%) of 109 cases of Eaton-agent pneumonia, the patients in these cases being more severely affected than the others.

It is not possible to distinguish Eaton-agent pneumonia from the other types on the basis of clinical findings alone.

John Fry

815. Vaccination against Measles. Part I. Preparation and Testing of Vaccines Consisting of Living Attenuated Virus

A. P. Goffe and G. D. LAURENCE. British Medical Journal [Brit. med. J.] 2, 1244-1246, Nov. 11, 1961.

The authors describe from the Wellcome Research Laboratories, Beckenham, Kent, the preparation and testing of four batches of live virus vaccine against measles, all of which were derived from different sublines of the Edmonston strain of measles virus. The parent strain had undergone many passages in human kidney and human amnion tissue cultures before being passaged 6 times in embryonated eggs. Batch 3C was prepared after a further 17 passages in chick embryo tissue cultures at 37° C., followed by 14 passages at 32° C. For the production of Batch 4A, after a preliminary 13 passages in chick embryo tissue cultures followed by 6 in embryonated eggs, the vaccine virus was passaged once in chick embryo tissue culture at 37° C. and 3 times at 32° C. Vaccines 8 and L, which were prepared in the U.S.A., had undergone 53 and 19 passages respectively in chick embryo tissue cultures. After freezing and thawing and clarification, Vaccines 3C and 4A were freeze-dried, as was also Batch 8 received from the U.S.A., as a liquid vaccine; Batch L was a liquid vaccine which was preserved frozen in solid carbon dioxide.

After the content of live virus had been determined each of the British vaccines was tested for potency by estimating the titres of antibodies evoked by inoculation of guinea-pigs. The degree of attenuation of virulence of the vaccines was assessed by the inoculation of monkeys. Difficulties were encountered in this test, as not only did some animals show evidence of recent previous infection, but also the criteria by which attenuation of the virus was gauged were poorly defined and hence difficult to measure. Tests for extraneous viral and bacterial agents yielded negative results. The freezedried vaccine was stable and little loss of titre occurred even after it was exposed to Nigerian sunshine for one hour.

Before use in the trial each British vaccine was inoculated into 3 adult volunteers, with no untoward results.

J. E. M. Whitehead

816. Vaccination against Measles. Part II. Clinical Trial in Nigerian Children

P. COLLARD, R. G. HENDRICKSE, D. MONTEFIORE, P. SHERMAN, H. M. VAN DER WALL, D. MORLEY, A. P. GOFFE, G. D. LAURENCE, and T. M. POLLOCK. *British Medical Journal [Brit. med. J.]* 2, 1246–1250, Nov. 11, 1961. 2 figs.

The effectiveness of three of the vaccines described above [see Abstract 815] was studied in three groups of Nigerian children all under 2 years of age: (1) of 24 children attending the infant welfare clinic of University College Hospital, Ibadan, none having a history of measles, the liquid Vaccine L was given to 18 and poliomyelitis vaccine to the other 6 as a control. (2) At the same clinic Vaccine 3C (dried) was given to 15 children, Vaccine 4A to 14, and poliomyelitis vaccine to 15. (3) The third study was carried out at the Wesley Guild Hospital, Ilesha, Nigeria, where 6 children received Vaccine 3C, 7 Vaccine 4A, and 9 (control group) received poliomyelitis vaccine. All vaccines were given subcutaneously.

After vaccination the children were examined daily for 15 days, except at Ilesha where the follow-up was incomplete. Blood samples taken at the time of inoculation and 3 to 6 weeks later showed a satisfactory antibody response in all the children vaccinated against measles. About 92% of these children developed pyrexia of 100° F. (37.8° C.) or higher during the period of observation; this occurred on the average about 7 days after vaccination and had an average duration of 3½ days. A morbilliform rash developed in 66% of the children, although in slightly more than half it was milder than in naturally acquired measles. In 8 of the controls pyrexial illnesses developed, but in only one were there signs and symptoms of natural measles. Of the 7 measles-vaccinated children admitted to hospital, 4 had illnesses attributable to the vaccine, including hyperpyrexia (one case), otitis media (one), and severe measles rash (2 cases). The clinical reactions to all three vaccines were similar. J. E. M. Whitehead

817. Vaccination against Measles. Part III. Clinical Trial in British Culldren

I. R. Aldous, B. H. Kirman, N. Butler, A. P. Goffe, G. D. Laurence, and T. M. Pollock. *British Medical Journal [Brit. med. J.]* 2, 1250–1253, Nov. 11, 1961. 1 fig., 9 refs.

The clinical and antibody response to three related measles vaccines was studied at the Fountain Hospital, London, and Queen Mary's Hospital, Carshalton, Surrey, in 77 mentally deficient children aged from 3 to 11 years, none of whom had demonstrable antibodies to measles virus before vaccination. They lived in self-contained wards housing between 20 and 50 patients, and at one hospital attended a common hospital school. The children were ranked by age in each ward and adjacent children in the ranks were allocated to one of three vaccination groups or to the control unvaccinated group. In all cases vaccination was by subcutaneous injection, the vaccines used being 3C, 4A; and 8, as previously described [see Abstract 815]. After being vaccinated in groups at 2-weekly intervals the children were ob-

served closely for 21 days, when a sample of blood was collected for estimation of antibody levels.

All the children showed a rise in antibody after vaccination, the levels being similar with all three vaccines. A morbilliform rash developed in 86%, while pyrexia developed during the follow-up period in 82%, and is described as "more than slight" in 66%. It persisted for one to 6 days, with an average duration of 2 days. By contrast only 4 of the 20 unvaccinated children became pyrexial. In 9 of the 57 vaccinated children the reactions were marked, 6 having an illness similar to natural measles and one developing bronchopneumonia. One death occurred on the 8th day in a child with a history of epilepsy who was well and apyrexial until the 7th day when he developed status epilepticus. In this case bronchopneumonia was found at necropsy, but no lesions characteristic of measles were observed in the lungs although typical measles giant-cells were present in the appendix. The authors conclude that although reactions after vaccination indicate that further attenuation of the vaccine strains of virus is required, the vaccine nevertheless produces an adequate antibody response, as was demonstrated not only by the production in vitro of neutralizing antibody but also by clinical evidence of immunity to reinfection by measles virus. This was shown when an epidemic of measles developed in one of the hospitals subsequent to the vaccination during which only one of the 34 vaccinated children developed the disease, whereas 8 out of 13 who had not been vaccinated did so. J. E. M. Whitehead

818. Assessment of the Therapeutic Effect of Xenaldial in Viral Hepatitis. (Valutazione dell'effetto terapeutico dello xenaldiale nella epatite virale)

F. MAGRASSI, M. COLTORTI, G. GIUSTI, A. DI SIMONE, and L. VALOROSO. *Minerva medica* [*Minerva med.* (*Torino*)] 52, 3137-3141, Sept., 15, 1961. 3 figs., 12 refs.

Previous investigations by the authors and others have shown that "xenaldial", a diphenyl keto-aldehyde, inhibited the growth of various types of virus in vitro and cured viral hepatitis in mice. At the University Polyclinic, Naples, the authors have used this drug in a dosage of 30 to 50 mg. per kg. body weight by mouth for 14 to 21 days in the treatment of patients with viral hepatitis, the therapeutic effect being assessed by determination of the serum enzyme levels before and after treatment. The value of the drug was confirmed by the rapid improvement in the signs of parenchymal liver damage and by the fact that relapses during treatment were prevented.

Franz Heimann

819. Virus Infections of the Respiratory Tract. [Review Article]

T. Anderson. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 1295-1300, Dec. 9, 1961. 2 figs.

820. Infectious Diseases: Annual Review of Significant Publications. [Review Article]

H. A. REIMANN. Archives of Internal Medicine [Arch. intern. Med.] 109, 60-96, Jan., 1962. Bibliography.

Tuberculosis

821. The Combination of Vaccination and Chemoprophylaxis against Tuberculosis. (Zur Kombination von Impf- und Chemoprophylaxe der Tuberkulose)
H. Spiess. Deutsche medizinische Wochenschrift [Disch. med. Wschr.] 86, 2162–2163, Nov. 10, 1961. 9 refs.

In the prophylaxis of tuberculosis the effects of vaccination with B.C.G. differ from those of treatment with chemotherapeutic agents. Thus while prophylactic treatment with isoniazid requires continuous administration of the drug, the protection afforded by B.C.G. vaccination persists for years. The author suggests, therefore, that a combination of these two methods might be of value in cases of suspected infection with, or known exposure to, tuberculosis.

In experiments carried out at the University of Gottingen 80 guinea-pigs were divided into four equal groups as follows: (1) a control group which was untreated; (2) the animals were vaccinated with 0.1 mg. of B.C.G.; (3) B.C.G. vaccination as above plus isoniazid in a dosage of 6 to 8 mg. per kg. body weight daily; and (4) vaccination as in Groups 2 and 3 and isoniazid in the same dosage, but begun 6 weeks later. The reaction to tuberculin was, with one exception, negative in all the animals in Group 3, but positive in 15 out of 20 animals in Group 4. Thus while the combined treatment suppresses vaccination allergy and protection against superinfection, this suppression can be avoided by performing B.C.G. vaccination 6 weeks before. The author recommends that in cases of suspected infection with tuberculosis isoniazid should be given immediately for at least 6 weeks. If the tuberculin reaction is then negative B.C.G. vaccination should follow, otherwise treatment with isoniazid is continued. Franz Heimann

822. The Swedish BCG Vaccine: Some Aspects on the Present Mode of Preparation and the Tuberculin Sensitivity 7 and 14 Years after Vaccination. [Monograph, in English]

O. Sievers and J. Sievers. Scandinavian Journal of Clinical and Laboratory Investigation [Scand. J. clin. Lab. Invest.] 13, 1-46, Suppl. 60, 1961. 9 figs., bibliography.

823. A Trial of Corticotrophin and Prednisone with Chemotherapy in Pulmonary Tuberculosis

A REPORT FROM THE RESEARCH COMMITTEE OF THE BRITISH TUBERCULOSIS ASSOCIATION. Tubercle [Tubercle (Lond.)] 42, 391–412, 1961. 3 figs., 28 refs.

This paper describes a trial which was undertaken by the British Tuberculosis Association in order to assess the effects of adding ACTH or prednisone to the therapeutic regimen. It was carried out on 346 patients with active pulmonary tuberculosis in whom the disease was believed to be of recent origin, the sputum was initially positive for tubercle bacilli, and who had received little (not more than 3 weeks) or no previous treatment. They were allocated at random to three groups as follows:

(1) a control group of 119 patients who were treated with 1 g. of streptomycin, 16 g. of PAS, and 300 mg. of isoniazid, all daily, for 6 to 12 months; (2) 111 patients who were treated as above but received in addition 30 i.u. of ACTH (corticotrophin) daily for the first 3 months; and (3) 116 patients who were treated as the controls plus 30 mg. of prednisone daily, also for 3 months. The assessments took place at intervals up to 12 months. The first patient entered the trial in September, 1957, and the last in July, 1959.

In a discussion of the results it is noted that although the patients in the control group receiving only bed rest and chemotherapy made excellent progress, there seems little doubt that in severely ill patients with extensive bilateral disease prednisone can be of great help. The immediate improvement, as judged by weight gain and fall in temperature and erythrocyte sedimentation rate, was significantly greater in those receiving prednisone than in the controls and the chest radiographs at 12 months also showed less disease. In the ACTH-treated group the same early improvement was noted, but it was not so marked as in the prednisone group. In all 3 groups the sputum of nearly every patient was negative by the end of 6 months. Hormone therapy, however, did not completely suppress hypersensitivity reactions to the antituberculous drugs. Moreover the hormones themselves can give rise to unpleasant side-effects, such as mental disturbances in those receiving ACTH. Watch has also to be kept for clinical "rebound' phenomena on withdrawing hormone therapy; these occurred in 6 (15%) of the patients given ACTH and in 34 (30%) of those given prednisone, but the symptoms lasted for only a few days. Paul B. Woolley

824. Long-term Results of Treatment of Cavitary Pulmonary Tuberculosis with a Combination of Pyrazinamide and Isoniazid. (Resultati a distanza del trattamento della tuberculosi polmonare cavitaria mediante l'associazione terapeutica pirazinamide isoniazide (Pz+INI)) C. Zucchetto. Rivista di patologia e clinica della tuberculosi [Riv. Pat. Clin. Tuberc.] 34, 656-678, Sept.-Oct., 1961. 18 figs., bibliography.

At the Guido Banti Sanatorium, Pratolino, Florence, 42 patients with recent tuberculous disease and 33 with chronic tuberculosis and cavitation were treated with 2 g. of pyrazinamide and 200 mg. of isoniazid daily; the maximum duration of treatment was 6 months. In those with recent disease radiological improvement was good in 59.5%, while in those with chronic disease the corresponding figure was 36.6%. Of 30 patients who had done well and who were observed for 26 to 41 months, in only 2 was there deterioration in the radiographs. Toxic effects of the drugs were few and mild.

[No bacteriological results are reported.]

Arnold Pines

Venereal Diseases

825. Studies on the Complement Activity in the *Tre- ponema pallidum* Immobilization (TPI) Test. A Comparative Study of the Immobilizing and Hemolytic Complement Activity. [In English.]

B. Hederstedt. Acta pathologica et microbiologica Scandinavica [Acta path. microbiol scand.] 53, 180–190, 1961. 4 figs., 11 refs.

In the treponemal immobilization (T.P.I.) test the treponemes are immobilized by syphilitic serum in the presence of complement and the persistence of excess complement at the end of the test period is demonstrated by its ability to lyse sensitized sheep cells. The reproducibility of the test was studied at the State Bacteriological Laboratory, Stockholm, using a very carefully standardized technique [for details of which the original paper should be consulted]. Tests were set up in duplicate on 16 days over a 5-week period using aliquots of the same pool of positive serum and of a pool of complement which had been stored at -60° C. Determinations of the serum dilution which immobilized 50% of the treponemes and of the 50% lysis titre of the complement showed very good reproducibility over the period of testing.

Tests were then performed using individual complements from 16 guinea-pigs and pools of complement from animals selected at random. No proportionality was found between the immobilizing activity and the haemolytic activity of the various complements tested. Sera from 10 patients with untreated or treated early syphilis which had a low titre of immobilizing antibody were then tested with two further pools of complement (E and F). These pools had almost equal haemolytic activity, but one (E) had previously been shown to have a higher immobilizing activity than the other (F). With Pool E, the T.P.I. test gave a positive result in 7 sera and a doubtful result in 3; with Pool F, the result was doubtful in 4 and negative in the remaining 6 sera. It was shown that the complement did not lose its immobilizing activity even after storage for one year at -60° C. Thus it is possible to enhance the sensitivity of the T.P.I. test by using complement which has been previously selected as having a high immobilizing activity.

A. E. Wilkinson

826. The Sensitivity of *N. gonorrhoeae* to Antibiotics.

O. RINGERTZ. Acta pathologica et microbiologica Scandinavica [Acta path. microbiol. scand.] 53, 173-179, 1961. 4 figs., 23 refs.

In the last few years physicians in Sweden have noted an increasing number of cases of gonorrhoea which fail to respond to the customary dose of 600,000 units of procaine penicillin. In this study 777 strains of gonococci isolated in the course of routine diagnostic work at the National Bacteriological Laboratory, Stockholm, during 1959-60 were tested for sensitivity against sulphonamide, penicillin, streptomycin, and tetracycline. Chocolate agar plates were flooded with a suspension of about 20 colonies of gonococci in 3 ml. of broth. After drying, paper disks containing 2.4 mg. of sulphonamide, 20 units of benzylpenicillin, 50 μ g. of streptomycin, or 50 μ g. of tetracycline were applied, the plates being left at room temperature for 3 hours for diffusion to occur and then incubated in an atmosphere containing 10% CO₂ for 24 hours. The minimum inhibitory concentrations were then calculated from the diameter of the inhibition zones.

Of the 777 strains 99% were sensitive to sulphonamide, most being inhibited by 0.5 mg, per 100 ml, or less, but 3 strains (0.4%) were highly resistant. The majority of the strains were sensitive to penicillin in concentrations of 0.06 unit per ml. or less, but 1.7% were sensitive only to 0.13 to 0.5 unit per ml. To streptomycin 97.9% were sensitive to a concentration of $4 \mu g$, per ml., but 9 strains (1.2%) were highly resistant and these often also showed a reduced sensitivity to penicillin. All the strains were sensitive to tetracycline, being inhibited by concentrations of 0.25 µg. per ml. or less. Some of the streptomycin-resistant strains were traced to the same source. The fact that all 9 strains appeared within a 3-month period during 1960, 5 of them within 18 days, indicated that these strains were epidemiologically stable and able to spread within a community. A. E. Wilkinson`

827. Epidemiological Aspects of Gonococcal Infections R. R. WILLCOX. Bulletin of the World Health Organization [Bull. Wld Hlth Org.] 24, 357-366, 1961. Bibliography:

828. Significance of Non-specific Genital Infection in Uvettis and Arthritis

R. D. CATTERALL. Lancet [Lancet] 2, 739-742, Sept. 30, 1961. 31 refs.

At the Institute of Ophthalmology, London, 211 males with uveitis were investigated for the presence of pus in the prostatic fluid, and it was found that 145 (68.7%) had either clumps of pus or more than 10 leucocytes per 1/12-inch (2.6 mm.) microscope field. This suggested chronic prostato-vesiculitis. In a group of 75 controls of the same age range selected from in-patients in the general medical and surgical wards of 2 teaching hospitals the incidence of chronic prostatitis was 14 cases (18.6%). Amongst the group of patients with uveitis Reiter's disease occurred in 45 (21.3%) and ankylosing spondylitis-in 26 (12.3%). In 7 patients plantar fasciitis or sacro-ilitis alone were found. It is suggested that chronic prostato-vesiculitis may be the underlying cause of anterior uveitis, Reiter's disease, ankylosing spondylitis, atypical sacro-iliitis, and plantar fasciitis.

G. W. Csonka

Tropical Medicine

829. Antibiotic Therapy in Tropical Sprue

T. W. Sheehy and E. Perez-Santiago. Gastroenterology [Gastroenterology] 41, 208-214, Sept., 1961. 3 figs., 39 refs.

Twelve Puerto Rican patients with tropical sprue were given 1 g. of tetracycline daily for 7 days followed by 1 g. of 'chloramphenicol daily for a further 7 days. A haematological remission, accompanied by a marked clinical improvement, occurred in 4 cases. Faecal fat excretion was reduced in 6 cases and the xylose excretion test improved in 7 cases following antibiotic therapy. The absorption of vitamin B_{12} labelled with 60 Co was unaffected and serum vitamin- B_{12} levels remained low. Jejunal biopsies showed moderate improvement in 4 cases and marked improvement in 2 others. M. Lubran

830. Home Treatment of Malaria in Children

W. I. B. Onuigho. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. toy. Soc. trop. Med. Hyg.] 55, 547-549, Nov., 1961. 10 refs.

To determine the part played by treatment at home in combating malaria, 200 children attending the out-patient clinic at the General Hospital, Enugu, Nigeria, were questioned about the drugs they had been given at home during the illness. It was found that the most popular medicaments were analgesics, followed by purgatives, antimalarial and antibacterial drugs, and indigenous medicines, in that order. The dosage of antimalarial drugs was inadequate in every case. The evidence suggested that children usually received active but misdirected treatment, and the author therefore urges that specially trained local personnel should teach the inhabitants "how to use the single-dose method of treating malaria with the appropriate drug". R. A. Neal

831. Paromomycin (Humatin) in Amoebic Infection

R. N. CHAUDHURI, T. K. SAHA, and N. ROY. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med. Hyg.] 55, 424-427, Sept., 1961. 7 refs.

In the animal studies and clinical trials here reported from the School of Tropical Medicine, Calcutta, paromomycin ("humatin") was tested first on guinea-pigs which had been experimentally infected with *Entamoeba histolytica*. The drug was given orally in a dosage of 75 mg. once a day for 5 days [equivalent to 150 to 250 mg. per kg. body weight]. Of 11 guinea-pigs so treated 8 responded to the drug, but 2 died from the infection and one relapsed, the remaining 5 being cured. In the 3 showing no response extensive amoebic ulcers were found in the caecum at necropsy.

Paromomycin was then given to 20 Indian patients suffering from intestinal amoebiasis, of whom 16 were suffering from dysentery, 2 were asymptomatic, and 2 gave a history of periodic diarrhoea. The drug was given

orally in a dosage of 150 mg. at 6-hourly intervals for 7 days. E. histolytica was not seen in the stools of 18 of the patients after the 6th day of treatment, but reappeared later in the stools of 4 patients. The drug did not affect the liver infection in 4 patients. A side-effect of the drug was diarrhoea, which subsided in 5 to 10 days, but it was sufficiently troublesome to necessitate discontinuation of therapy in one patient. R. A. Neal

832. Paromomycin in the Treatment of Amoebiasis in Nyasaland

E. D. WAGNER and H. S. BURNETT. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med. Hyg.] 55, 428-430, Sept., 1961. 5 refs.

The authors report from Loma Linda University, Los Angeles, a study of the amoebicidal activity of the broadspectrum antibiotic paromonycin ("humatin") in the treatment of chronic infections due to *Entamoeba histolytica* in Nyasaland. In all, 53 patients, 42 males and 11 females (including 4 children aged 7 to 12 years), were treated with the drug in doses ranging from 25 to 4.7 mg. per kg. body weight per day for either 3 or 5 days.

The cases were of the chronic type of amoebiasis, and the mild abdominal symptoms present in most cases may have been due to an associated helminth infection, from which many of the patients suffered. Of the 21 patients treated with paromomycin in a dosage of 25 mg. per kg. for 5 days the stools of 17 became negative at 12 weeks, while the 4 positive results were considered to be due to reinfection. Of the 13 patients given 7.5 mg. per kg. for 3 days the stools of 12 became negative, with one case of reinfection, at 12 weeks. Thus both these dose levels of the drug were effective. No toxic side-effects were observed. In the one case in which treatment failed the dosage was 4.7 mg. per kg. for 3 days, which is probably below the effective range.

R. A. Neal

833. The Treatment of Amoebiasis with "Resotren Compound"

A. Z. SHAFEI. Journal of Tropical Medicine and Hygiene [J. trop. Med. Hyg.] 64, 282-285, Nov., 1961. 23 refs.

"Resotren" (cloquinate) is a chemical combination of 2 molecules of chiniofon with one molecule of chloroquine. When given by mouth about 50% is absorbed and exerts its action through the plasma, the remaining 50% exerting a contact action in the lower bowel. It has been reported to give a cure rate of 60 to 90% in amoebiasis. The present author, however, has found it to be poorly tolerated and has tried in its place "resotren compound", in each tablet of which 200 mg. of chloroquine and 300 mg. of diodoquin are added to 75 mg. of the original resotren. He gave it in doses of

two tablets thrice daily for 7 days, followed by one tablet thrice daily for another week. He claims that it was better tolerated than plain resotren and that 86% of 86 patients, including 27 with acute and 59 with chronic intestinal amoebiasis, were cured. It is also stated to be effective in hepatic amoebiasis.

Clement C. Chesterman

834. Electrocardiographic Changes during Emetine Treatment of Egyptian Children with Amoebic Dysentery S. AWWAAD, M. ATTIA, and M. REDA. Journal of Tropical Medicine and Hygiene [J. trop. Med. Hyg.] 64, 286–287, Nov., 1961. 8 refs.

At the Abbassia Children's Hospital, Cairo, 33 children aged 2 to 12 years were treated for acute amoebic dysentery with subcutaneous injections of emetine, 1 0 mg. per kg. body weight for 6 days. An electrocardiogram was recorded before and after treatment and the only significant change observed was an inversion or slightly lessened amplitude of the T wave in the right precordial lead in about one-third of the cases. The authors conclude that emetine in these doses is safe and effective and that no other drug is required for the treatment of children with amoebic dysentery.

Clement C. Chesterman

835. Measurement of Portal Pressure in Bilharzial Cirrhosis: Its Value in Determining the Relation of Portal Hypertension to the Various Clinical Aspects of the Disease

M. FAYEZ and S. AZIZ. Journal of the Egyptian Medical Association [J. Egypt. med. Ass.] 44, 345-357, 1961. 12 refs.

This investigation was carried out at Kasr-el-Aini Faculty of Medicine, Cairo, on 30 male patients whose age varied between 18 and 55 (average 34) years. Among the measurements made were that of portal pressure by percutaneous splenic puncture (full details of the technique employed being given), the pressure in the antecubital vein, and the pressure in anterior abdominal veins. Urine and stools were examined, the blood picture investigated, and various tests of hepatic function carried out. The patients were divided into two groups, each of 15 patients, according to whether ascites was present or not.

In the patients without ascites the liver was enlarged 1 to 4 finger breadths below the costal margin, and the spleen 1 to 7 finger breadths. The portal venous pressure was 310 to 738 mm. (mean 557 mm.) H₂O, compared with a pressure of 54 to 208 (mean 156) mm. H₂O in 23 control subjects. In the antecubital vein the pressure was about the same in patients and controls, namely, 28 to 144 (average 86) mm. H₂O. 'In the patients the plasma total protein level was normal, but the albumin: globulin ratio was slightly decreased. Except for one case, in which there was oedema and a collateral circulation, the results of hepatic function tests were normal. All these patients had hypochromic anaemia.

In the 15 patients with ascites the liver was shrunken in 4, but in the others it was enlarged 1 to 3 finger breadths below the costal margin; the splenic enlargement was 3 to 12 finger breadths. Ascites was slight in

3 cases, moderate in 4, and marked in 8, but was not tense in any patient; in over half of the cases there was peripheral oedema. The portal venous pressure was 560 to 1,050 (average 810) mm. H₂O; the pressure in the antecubital veins was normal. The plasma total protein value was 5 to 8.5 g. per 100 ml. and in all cases the albumin globulin ratio was reversed. Liver function tests showed that nearly all the patients in this group had hepatic deficiency. The haemoglobin value was 22 to 74% of normal. In general no definite correlation could be established between the size of the liver or spleen and the portal venous pressure; but a high portal pressure was usually accompanied by a contracted liver.

The authors discuss the mechanism of the formation of ascites.

W. H. Horner Andrews

836. Effect of Diuretics on the Portal Venous Pressure in Bilharzial Hepatic Fibrosis with Ascites

M. FAYEZ and S. AZIZ. Journal of the Egyptian Medical Association [J. Egypt. med. Ass.] 44, 425-436, 1961.

This study was carried out at the Kasr-el-Aini Faculty of Medicine, Cairo, on 18 male patients aged 16 to 46 years who were suffering from bilharzial hepatic fibrosis with ascites [as described in Abstract 835]. They were given a salt-poor diet [no figure is given for daily salt intake] and observed for a control period of 3 to 5 days, after which one of three diuretics was given for 15 days and various observations made, notably determination of the portal venous pressure and the plasma albumin level.

In the 6 patients who received 2 ml. of the mercurial diuretic. "salyrgan" (mersalyl) intramuscularly twice weekly the mean portal venous pressure, measured by the intrasplenic route, before treatment was 790 mm. H₂O, but one day after the beginning of treatment it had fallen to a mean of 632 mm. H₂O and after 15 days to 515 mm. H₂O, only one patient failing to show a good response. In the 6 patients who received 375 mg. of acetazolamide daily the initial mean portal venous pressure of 803 mm. H₂O fell to 656 mm. after one day and to 563 mm. H₂O after 15 days, while of the 6 patients treated with hydrochlorothiazide in a dosage of 150 mg. daily the corresponding values for mean portal venous pressure were 786, 634, and 606 mm. H₂O.

The pressure of the ascitic fluid, which was measured at the same time, decreased in nearly all cases with treatment, though the fall was less than that in the portal venous pressure, and in 2 cases in which the latter fell the ascitic fluid pressure actually rose. All three diuretic drugs produced an immediate fall in venous pressure in the antecubital vein, which after 15 days was still lower than the pretreatment value, although in 7 cases it was higher than that at one day. There was a loss of body weight in all except 3 patients, but the plasma albumin and globulin levels showed little change. The authors conclude that diuretics are of value in the treatment of bilharzial hepatic cirrhosis with ascites or bleeding from oesophageal varices.

W. H. Horner Andrews

Allergy

837. Difficulties in Weaning in Steroid Treatment of Asthma

J. P. KNOWLES. British Medical Journal [Brit. med. J.] 2, 1396-1399, Nov. 25, 1961. 11 refs.

The difficulty of withdrawing steroid therapy from asthmatic patients after a relatively prolonged course of steroids is now well known and although many authors have mentioned the difficulty, none appears to have specifically investigated the problem. In this retrospective study carried out at University College Hospital. London, the author records observations on 135 asthmatic patients aged 13 to 75 years who had been treated with steroids for various periods up to 8 years. The average duration of treatment was 27.7 months, while the average duration of the asthma before treatment was 17-6 years. Up to 1956 cortisone and ACTH (corticotrophin) were the main steroids used, but since 1957 the newer analogues had been employed. Of the 135 patients 102 were still taking steroids, whereas 33 had been weaned from these preparations. In all, 66 patients (48.9%) had received continuous treatment, 43 (31.9%) repeated courses, 10 (7.4%) a single course, 10 (7.4%) failed to show any response, and 6 (4.4%) had seasonal asthma associated with hay fever and were treated during the summer months only.

It was found to be easiest to wean patients with seasonal asthma; on the other hand those whose asthma started after the age of 30 relapsed readily and were likely to require continuous treatment. In 13 cases treatment was stopped because of complications, these including dyspnoea (5 cases), psychological disturbances (5), pregnancy (1), untoward reactions to ACTH (1), and renal tuberculosis (1). There were 5 deaths, one patient dying from pneumonia, one from primary amyloidosis, and 3 in status asthmaticus; of these last, one was receiving prednisone at the time of death, one had received a course of steroids 7 months before she died, and one was receiving steroids but the asthma had been inadequately controlled. R. S. Bruce Pearson

838. Adrenaline and Status Asthmaticus B. BROOM. Lancet [Lancet] 2, 1174-1176, Nov. 25, 1961. 17 refs.

The standard procedure for administration of adrenaline in status asthmaticus is a subcutaneous injection of 1 minim (0.06 ml.) a minute of the hydrochloride up to a total dose of 3 to 6 ml. The author of this paper from the Middlesex Hospital Medical School, London, describes his experience in the domiciliary management of 24 patients with severe acute bronchial asthma, 15 of whom were considered to be suffering from status asthmaticus. In 19 the intramuscular injection of 2 to 5 ml. of adrenaline hydrochloride (1/1,000) over a period of 5 to 15 minutes gave complete and lasting relief within 30 minutes. In 3 patients a second injection was

necessary before recovery and in 2 given respectively 8 and 10 ml. there was no response. Unpleasant side-effects, which occurred in all except 6 cases, included tachycardia (in 18), vomiting (16), pallor, headache, and sweating (10), extrasystoles (5), and tremor and anxiety (2). The injections caused "considerable pain".

Attention is drawn to published reports of death from overdosage of adrenaline if this is given too fast or intravenously. A lethal dose may be as low as 4 mg. (4 ml. of 1/1,000 solution) but is usually 10 mg. or more.

[This procedure is worth a trial, especially in view of the author's statement that it gave lasting relief.]

R. S. Bruce Pearson

839. A New Function of Gamma Globulins. Their Protective Action against Hypersensitivity Phenomena. (Sur une nouvelle fonction des gamma-globulines. Leur action protectrice contre les phénomènes d'hypersensibilité)

B. N. HALPERN. Presse médicale [Presse méd.] 69, 1991-1994, Oct. 28, 1961. 7 figs., 10 refs.

In this investigation carried out at the Department of Experimental Medicine of the Collège de France, Paris, it was shown that y globulins of some mammals interfere with the sensitization process in guinea-pigs. Passive anaphylaxis was induced in pitro in isolated guinea-pig gut after the tissue had been soaked in rabbit serum containing antibodies induced by ovalbumin injections. The anaphylactic contraction was prevented by previous treatment of the tissue with γ globulins prepared from rabbit, guinea-pig, or human serum (0.5 mg. per ml.), but not from the serum of the horse, cow, rat, or chicken. On the other hand, the anaphylactic contraction was increased by dialysing the tissue against saline (to remove the tissue v globulins) before immersion in the serum containing the antibody and challenge with the antigen (ovalbumin).

Similar tests carried out *in vivo* with the rabbit serum containing the antibodies showed that human or rabbit γ globulins (300 mg. injected intraperitoneally) prevented the general passive anaphylactic reaction in guinea-pigs. The local cutaneous passive anaphylactic reaction was also prevented by pretreatment with human, rabbit, or guinea-pig γ globulins.

G. B. West

$840. \ \,$ The Immunology of the Blocking Antibody in Ragweed Pollenosis

H. S. Bernton and D. C. CHAMBERS. Journal of Allergy [J. Allergy] 33, 26-34, Jan.-Feb., 1962. 10 refs.

841. Antitussive Medication in Asthma, Emphysema and Chronic Bronchitis. [In English]

N. E. Silbert. Acta allergologica [Acta allerg. (Kbh.)] 16, 232-253, 1961. 12 refs.

Nutrition and Metabolism

842. The Development of Hypervitaminosis D in the Employment of Synthetic Preparations of Vitamin D. (К вопросу о развитии гипервитаминоза D при применении синтетических препаратов витамина Д) А. М. Hvul', Ja. М. Gusovsku, and V. P. Vendt. Педиатрия [Pediatrija] 40, 34–39, Nov., 1961. 11 refs.

Experiments on rats given a very high dosage of vitamin D₂ (calciferol) showed that the vitamin in an alcoholic solution was toxic in only two-thirds of the dosage required to produce similar symptoms when it was given as a powder, the toxic dose in alcohol being 480,000 i.u. compared with 625,000 i.u. in powder form. The pathological changes observed included perivascular haemorrhages in the kidneys, liver, and heart, and in 2 cases foci of pneumonia appeared in the lungs. In 5 out of 12 cases calcium deposits in various organs were found. Similar changes were observed when the vitamin was administered in doses of 300,000 and 200,000 i.u.

Clinically, 2 children with very severe rickets were treated with a total dose of 2,700,000 i.u. over 8 days without any sign of toxic symptoms; 600 other children with rickets also received large doses—though less than a half of the above—with no ill effects. It seems that in the presence of deficiency calciferol can be given in a dosage very much higher than that which can be tolerated by healthy individuals. However, if it is given in powder form and not in alcoholic solution, even the latter can tolerate much more than the usual therapeutic dose, except in individual cases of susceptibility.

L. Firman-Edwards

843. Theory of the Use of Arteriovenous Concentration Differences for Measuring Metabolism in Steady and Non-steady States

K. L. Zierler. Journal of Clinical Investigation [J. clin. Invest.] 40, 2111-2125, Dec., 1961. 5 figs., 11 refs.

844. Studies of Serum Desmosterol Levels in Hyper-cholesteremic Subjects Treated with Triparanol (MER-29) B. A. SACHS and L. WOLFMAN. American Journal of Clinical Nutrition [Amer. J. clin. Nutr.] 9, 760-763, Nov.—Dec., 1961. 2 figs., 10 refs.

Discussing the disadvantages of the treatment of hypercholesterolaemia by the inhibition of cholesterol biosynthesis the authors point out that if such inhibition is produced at an early point in the cholesterol metabolic pathway (as occurs with benzmalecene) it leads to an accumulation of triglycerides in the serum, probably owing to the diversion of available acetate from cholesterol synthesis to triglyceride synthesis: on the other hand when the inhibitor acts late in the pathway, as for example does triparanol, there is an accumulation of the cholesterol precursor desmosterol in the serum. In view of the possible atherogenic action of this precursor,

which closely resembles cholesterol, the authors have observed the desmosterol levels in 10 patients with hypercholesterolaemia who were given triparanol in daily doses of 1,000 to 1,500 mg. at the Montefiore Hospital, New York, for 5 to 13 months.

The serum cholesterol level fell in all subjects, the average fall being 37%. Desmosterol was not demonstrable in the serum of these patients before treatment, but during administration of triparanol the serum desmosterol level rose by varying amounts, the mean value representing some 37% of the total serum sterol content. The total sterol level itself (that is, cholesterol plus desmosterol) fell in all subjects by a mean of 17%. The authors conclude [after a stimulating and highly controversial discussion] that it is not yet known whether the presence of desmosterol in serum in these amounts can produce harmful effects.

Z. A. Leitner

845. Porphyria in the African: a Study of 100 Cases N. McE. LAMONT, M. HATHORN, and S. M. JOUBERT. Quarterly Journal of Medicine [Quart. J. Med.] 30, 373-392, Oct., 1961. 18 figs., 30 refs.

This paper from King Edward VIII Hospital, Durban, reports a full-scale study of 100 cases of porphyria in Africans, of which 85 were consecutive and unselected. Two unusual features were the paucity of evidence of genetic origin and the remarkably uniform clinical pattern; the authors confirm the fundamental difference between the pattern of porphyrin excretion in these subjects and that in white South Africans as previously reported by other workers. Clinically, most of the patients showed cutaneous bullae, hyperpigmentation, and hypertrichosis: the liver was frequently enlarged. and about half the patients had peripheral neuritis. In the majority of cases the symptoms of porphyria were benign and incidental to other disease, but were of relatively recent onset when first investigated. In all the patients some abnormality of liver function was found on laboratory investigation, and in the specimens from the 28 on whom liver biopsy was performed fibrotic lesions were seen.

A history of consumption of a mainly maize diet and of kaffir beer and raw spirits to excess was frequent. The porphyrin excretion showed a predominance of urinary uroporphyrins and closely resembled that reported by Barnes (S. Afr. med. J., 1959, 33, 274), while the cutaneous lesions were similar to those observed in the series of patients with "toxic porphyria" recently reported from Turkey (Cetingil and Özen, Blood, 1960, 16, 1002), in which hexachlorobenzene was the drug incriminated.

The authors suggest that porphyria in the African is an acquired condition probably due to the consumption of ethyl alcohol associated with particular dietary habits.

B. M. Ansell

Gastroenterology

846. Management of Gastroenteric Gas Syndromes P. C. Pellegrino and H. B. Silberner. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 450-458, Oct., 1961. 22 refs.

Symptoms due to the accumulation of gas in the gastrointestinal tract, which is normally removed physiologically, may occasionally persist because the gas is entrapped as a froth within "membranes" composed of food materials or secretions. This paper describes a form of treatment for this condition in which gastro-intestinal enzymes are administered together with a silicone, dimethylpolysiloxane (DPS), a substance that has recently been used in gastroscopy as an effective means of reducing the froth which interferes with gastroscopic vision. The anti-foam action of DPS is based on its low surface tension, which enables it to rupture the gas-enveloping membrane by altering the interfacial tension and so releasing the entrapped gas which can then be eliminated in the normal manner. DPS requires to be specially activated, that is, emulsified into a hydrophilic form by means of bile acids; it is pharmacologically inert and is not absorbed from the intestine.

The preparation ("phazyme") used in this trial consists of an outer layer containing, for immediate availability in the stomach, 100 mg. of pepsin, 25 mg. of diastase, and 20 mg. of activated DPS, and an inner enteric-coated core, for release in the intestine, containing 240 mg. of pancreatin and 40 mg. of activated DPS. The dosage was one tablet with each meal and, if necessary, an additional tablet at bedtime. The treatment was given to 82 patients, of whom 69 had symptoms of gas distress without organic disease, 12 had symptoms associated with a gastro-intestinal lesion, and one had symptoms associated with cardiovascular disease. The treatment was given for various periods ranging from 7 to 238 days (mean 62 days). Patients whose symptoms were functional received the test preparation as the only treatment; those with organic disease received in addition the appropriate therapeutic measures. Satisfactory relief of symptoms was obtained in 70 patients (85%), including 12 of the 13 patients with organic disease. There were no adverse reactions in any of the patients.

Joseph Parness

847. Gastroduodenal Ulceration and Massive Hemorrhage in Patients with Leukemia, Multiple Myeloma, and Malignant Tumours of Lymphold Tissue

J. S. CORNES, T. G. JONES, and G. B. FISHER. Gastro-enterology [Gastroenterology] 41, 337-344, Oct., 1961. 35 refs.

The clinical and necropsy records of 585 patients with leukaemia, multiple myeloma, or malignant lymphoma were examined to try to determine the nature and incidence of gastroduodenal ulceration and the cause of massive gastroduodenal haemorrhage in patients dying of

these disorders. The patients were taken from a combined series of 14,944 consecutive necropsies performed at the Postgraduate Medical School of London and the Westminster Medical School, London.

Peptic ulcers were discovered in 32 patients (5.5%). They were commonest in patients with monocytic leukaemia (3 of 33 patients) and multiple myeloma (5 of 41 patients), and least common in those with lymphatic leukaemia (one of 58 patients) and Hodgkin's disease (5 of 132). The onset of malignant disease apparently preceded that of peptic ulceration in 23 patients; 17 of these had chronic gastric ulcers, 4 chronic duodenal ulcers, one chronic ulcers of the stomach and duodenum, and one acute gastric ulcer. Gross tumour deposits in the stomach or duodenum were found in 15 of the 264 patients with leukaemia, in 50 of the 280 patients with malignant lymphoma, and in none of those with multiple myeloma. In 9 patients with leukaemia and in 36 with malignant lymphoma the tumours were ulcerated, the total incidence of tumour ulcers being 7.4%. These ulcers in malignant lymphoma were often large and in 16 of the 36 cases they measured more than 3 cm. in their largest surface diameter. Symptoms suggestive of gastroduodenal involvement had been present in 32 cases and in 3 they were sufficiently severe to warrant palliative gastrectomy.

Massive haemorrhage into the upper gastro-intestinal tract occurred in 17 patients with leukaemia, in 13 with malignant lymphoma, and in none with multiple myeloma. In 9 patients, mostly with leukaemia, it was attributed to acute gastric erosion, in 8 patients it was due to peptic ulceration, and in 8 to secondary tumour ulceration. Four additional patients with acute leukaemia and one with Hodgkin's disease bled as a result of thrombocytopenia.

The authors conclude that gastroduodenal ulceration is not rare in leukaemia, multiple myeloma, and malignant lymphoma, and that in some cases it is the most important clinical feature of the disease.

Elrian Williams

848. Chronic Gastritis. I. Correlation of Gastroscopic Findings with Biopsy. [In English]

Z. MARATKA and J. ŠETKA. Gastroenterologia [Gastroenterologia (Basel)] 96, 211-216, 1961. 13 refs.

The authors, who report from the 2nd Medical Clinic, Charles University, Pragué, have attempted to correlate the gastroscopic findings with the results of biopsy in 120 cases of chronic gastritis. While 1,500 gastroscopic examinations and 500 biopsies have been carried out altogether, these 120 cases were selected as being suitable for study on the grounds that the two examinations were accomplished close to each other.

Poor correlation was found between gastroscopic and biopsy findings, and this applied to all types of gastritis, including the hypertrophic and atrophic forms. The authors conclude that "gastritis" remains a pathological label, and that it would be more helpful for the gastroscopist to describe the appearances by such terms as "granular mucosa" and "impression of atrophy".

I. McLean Baird

LIVER AND GALL-BLADDER

849. The Control of Gastro-intestinal Hemorrhage in Cirrhosis by Combined Adrenocortical and Estrogenic Therapy

H. J. ROBERTS. Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.] 9, 976-997, Nov., 1961. Bibliography.

The author reviews the methods available for controlling gastro-intestinal haemorrhage in cirrhosis, which is reputed now to be one of the 10 leading causes of death in the United States; these include blood transfusion, vitamin and drug therapy, venous shunt operations, and balloon tamponade. He then describes the treatment of 5 cirrhotic patients with persisting gastrointestinal haemorrhage. These were given repeated slow intravenous infusions, from 6-hourly to once-daily, of 20 mg. "premarin intravenous", which contains oestrogen in a naturally occurring water-soluble conjugated form. The steroid used was cortisone acetate, 75 to 100 mg. intramuscularly, or latterly dexamethasone, 4 to 8 mg, intramuscularly or intravenously. in both cases at 6- to 8-hour intervals, the dosage being gradually reduced as the bleeding subsided. Supplementary antacids were given to prevent steroid-induced ulcers. Control of haemorrhage was achieved usually within 12 to 16 hours, although other methods of treatment had failed.

Oestrogen given by the intravenous route does not appear to cause the retention of water and fall in sodium and chloride excretion which usually follow its intramuscular or oral administration. The author discusses in detail the possible haemostatic action of oestrogens and of adrenocortical steroids and examines the interrelationships between adrenocorticosteroid and oestrogen metabolism. Discussing the fear that a damaged liver might not be able to inactivate the oestrogen, he states his belief that it tenaciously retains this ability [though there were complications in his cases suggesting that it had been lost].

J. N. Agate

850. Portal Circulation in Hydatid Cyst of the Liver V. GILSANZ, M. GALLEGO, and P. CALLE YUSTE. Archives of Internal Medicine [Arch. intern. Med.] 108, 540-547, Oct., 1961. 5 figs., 2 refs.

In this communication from the Department of Internal Medicine, University of Madrid, the authors demonstrate the value of serial splenoportography as used in a study of 11 cases of hydatid cyst of the liver due to *Taenia echinococcus*, infestation with which is very prevalent in Spain. Ten of the cysts were in the right lobe of the liver and only one in the left lobe. It was found that the cyst often caused displacement of the portal hilum and produced lacunar dilatation and displacement of secondary divisions of the hepatic vein,

with T-branch formations; there was also absence of vascular filling in the area of the cyst. In every case in which the cyst was located by splenoportography the site was confirmed either at laparotomy or necropsy. The intrasplenic pressure was raised in all cases. Determination of the ether spleen-lung circulation time (by a method described) showed that only in cases in which the hilum and hence the splenic vein were compressed was this time prolonged as compared with the arm-lung circulation time. The authors point out that cancer of the liver does not give rise to lacunar dilatations and T formations and claim that these signs are diagnostic of hydatid cyst.

Arnold Pines

851. Parenchymal Siderosis in Patients with Cirrhosis after Portasystemic-shunt Surgery

W. A. TISDALE. New England Journal of Medicine [New Engl. J. Med.] 265, 928-932, Nov. 9, 1961. 4 figs., 15 refs.

Of 20 patients at the Massachusetts General Hospital, Boston, subjected to porta-systemic (usually splenorenal) venous anastomosis, in respect of whom hepatic tissue was available for histological examination before and after surgery, 2 (females) with post-necrotic cirrhosis had extensive iron deposits in the parenchymal cells of the liver and pancreas at the time of death, 2 and 9 years respectively after operation. In one of the cases iron was also found in the myocardium, adrenal cortex. and renal tubules. Neither patient had diabetes or heart failure. The amount of blood transfused (8.5 litres and 10 litres respectively) was insufficient to explain the findings. In contrast, siderosis was not observed in a comparable series of 21 patients with cirrhosis of the liver who were not subjected to porta-systemic shunt, and the author suggests that the operation in some way increased the amount of iron absorbed from the gastro-P. C. Reynell intestinal tract.

852. Posthepatitic Hyperbilirubinaemia. (Die posthepatitische Hyperbilirubinamie)

F. MARGADANT. Helvetica medica acta [Helv. med. Acta] 28, 663-680, Nov., 1961. Bibliography.

This paper from the Cantonal Hospital, Chur, Switzerland, gives an account of present-day views upon the production and excretion of bilirubin, with a survey of the literature and a discussion of the mechanism of bilirubin conjugation as a hepatocellular activity. Hyperbilirubinaemia as a defect of the bile transferase system is described as part of a transport disturbance of bilirubin. Observations upon 20 patients with indirect intermittent hyperbilirubinaemia are recorded, in 14 of whom it was of the posthepatitic type and in 6 of the inborn "Gilbert-Meulengracht" type. One case of the Dubin-Johnson syndrome was also noted. The chemical and laboratory findings in typical posthepatitic hyperbilirubinaemia are described and tables are given in which the characteristics of other types of hyperbilirubinaemia are drawn up for purposes of differential diagnosis. The author considers that the cases which follow hepatitis are due to a deficiency of transferase in the liver cells and considers that such cases are far from

rare. They are diagnosed by the occurrence of intermittent attacks of jaundice with increase in the indirect serum bilirubin level in the absence of any detectable liver damage as shown by normal liver biopsy and function tests. The author's cases were observed for periods up to 15 years and in no instance did cirrhosis develop or any evidence of haemolysis. In most of the cases the attacks became milder and in many ceased completely. It is important to reassure the patient as to the harmless nature of the jaundice, even though the liver and spleen may at times enlarge and there may be dyspeptic and nervous symptoms. Only 5 cases are described in detail, 4 of the posthepatitic type and one of the "Gilbert-Meulengracht" type.

Thomas-Hunt

INTESTINES

853. Life History of the Carcinoid Tumour of the Small Intestine

C. G. MOERTEL, W. G. SAUER, M. B. DOCKERTY, and A. H. BAGGENSTOSS. Cancer [Cancer (Philad.)] 14, 901–912, Sept.—Oct., 1961. 4 figs., 25 refs.

This long and detailed study of the pathology, symptomatology, and treatment of 209 cases of carcinoid tumour of the small intestine is presented from the Mayo Clinic, Rochester, Minnesota. The diagnosis was made only at necropsy in 137 cases and at laparotomy in 72. The primary lesion was usually "silent", though occasionally it led to intussusception or ulceration with bleeding. Multicentricity of origin was much more frequent than with any other malignant tumour, and the incidence of other primary cancers of a different nature was high (53%). Symptoms were usually associated with the presence of metastases. The symptoms were often vague, however, and sometimes simulated a functional complaint. The most frequent were abdominal pain and intestinal obstruction, these being found in 43% of the 56 patients with symptoms. An inordinately long history of symptoms is looked upon as characteristic.

The prognosis for this condition is better than for any other malignant tumour, the 5-year survival rate for all operable tumours being 68%. A simple bypassing operation usually abolished the abdominal pain and diarrhoea. The authors state that resection of the largest possible amount of tumour should be performed irrespective of the presence of secondary growths. This series included 14 cases of carcinoid syndrome caused by the excessive secretion of 5-hydroxytryptamine (serotonin) and 13 of these patients showed the characteristic flush.

[This paper should be read in its entirety by those interested in the subject, since only the salient points can be mentioned in an abstract.]

R. Schneider

854. Antibodies to Cow's Milk in Ulcerative Colitis J. G. Gray. *British Medical Journal [Brit. med. J.]* 2, 1265-1266, Nov. 11, 1961. 7 refs.

In view of the reports in the literature on the possibly important role of allergy to milk in the pathogenesis of ulcerative colitis, the author, working in the Department of Experimental Pathology, University of Birmingham, examined sera from 40 patients with ulcerative colitis, 40 hospital patients with non-alimentary conditions, and 40 healthy subjects for antibodies to milk protein, the sensitive tanned erythrocyte haemagglutination method being used. The percentage of patients whose serum contained antibodies to cow's milk protein was essentially the same in the three groups, but the titres in patients with ulcerative colitis were significantly higher than those in patients in the other two groups.

The presence of antibodies to ovalbumin was similarly studied, but no significant difference was observed between the groups in respect of either the proportion of patients with serum antibodies to the protein or the antibody titres.

A. Gordon Beckett

855. Ulcerative Colitis with Onset after the Age of Flity D. H. LAW, H. STEINBERG, and M. H. SLEISENGER. Gastroenterology [Gastroenterology] 41, 457-464, Nov., 1961. 21 refs.

The course of ulcerative colitis with onset after the age of 50 years was studied at the New York Hospital-Cornell Medical Center, New York, in 30 patients (15 male and 15 female). The authors found that there was a significant incidence of emotional trauma shortly before the onset of the disease and that in a disproportionately large number of cases symptoms were first noted after physical trauma. In 14 cases the disease was limited to the rectum or rectosigmoid colon; none of the patients had enterocolitis. Incorrect diagnoses, usually of malignant disease or diverticulitis, were common initially (in 22 out of the 30 cases) and were the result in most instances of misinterpretation of the sigmoidoscopic findings; all the patients had symptoms referable to colonic disease, these being similar to those seen in younger patients with ulcerative colitis, except for the occasional lack of a febrile response. As might be expected, associated diseases, especially arteriosclerosis, were common.

The response to adrenal corticosteroids was good (9 out of 17 patients having complete remission of symptoms), but care was necessary because of the associated diseases. The results of surgery (10 patients) appeared to be inconsistent, due largely to misdiagnosis and "hesitancy to perform definitive operations in the older age group". In the 5 patients subjected to planned operations the results with regard to the colitis were good, although one patient had ileostomy dysfunction and one a severe postoperative paranoid reaction. Transection or anastomosis of a diseased colon in 4 patients with undiagnosed ulcerative colitis led to moderate or severe exacerbation of the disease.

The authors conclude that the management of ulcerative colitis in patients over 50 is not more difficult than in younger patients, but the course of the disease is affected adversely by delay in diagnosis and by concomitant disorders.

A. Gordon Beckett

856. Ulcerative Colitis. [Review Article] T. P. Almy. Gastroenterology [Gastroenterology] 41, 391-400, Oct., 1961. Bibliography.

Cardiovascular System

857. Hypertension and Edema in the Aged: Observations on the Use of a Meprobamate-Hydrochlorothiazide Combination

W. W. BARE and H. L. BAIRD. Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.] 9, 968-975, Nov., 1961. 4 figs., 3 refs.

The oral use of meprobamate (200 mg.) and hydrochlorothiazide (25 mg.) in a single tablet was tested for a period of 3 months on 54 geriatric patients suffering from oedema or hypertension, or both, at the Methodist Home for the Aged, Philadelphia, Pennsylvania. Patients whose blood pressure, either systolic or diastolic, exceeded 150/90 mm. Hg were considered to have hypertension. After treatment there was a reduction in the average systolic, diastolic, and pulse pressures, especially in patients with higher blood pressure initially. Diuresis occurred in the oedematous patients, but the average loss of weight in 3 months was only 4 lb. (1.8 kg.). There was a rise rather than a fall in the serum potassium levels, because citrus-fruit juices were allowed. The authors conclude from the findings that this combination of drugs is an effective and safe antihypertensive and diuretic agent.

[The oedematous and hypertensive patients might have been studied in separate groups. It is not clear whether there was any clinical indication for attempting to lower the blood pressure or what the causes of the oedema were.]

J. N. Agate

858. Giant-cell Arteritis without Headache G. A. MACGREGOR. Lancet [Lancet] 2, 1160-1163, Nov. 25, 1961. 10 refs.

The author has investigated 12 cases of acute myalgia with constitutional symptoms. All were benefited by corticosteroid therapy. In none of the cases was there headache or evidence of temporal arteritis, but the author suggests that the aetiology of the two conditions may be similar. He postulates that small patches of atheroma give rise to the typical histological reaction in the vessel wall and thus to the symptoms.

J. B. Wilson

859. The Relationship between Diet and Atherosclerosis in Ceylon

T. W. WIKRAMANAYAKE and R. PANABOKKE. American Journal of Clinical Nutrition [Amer. J. clin. Nutr.] 9, 752-759, Nov.—Dec., 1961. 27 refs.

A review of the results of nutritional surveys carried out in Ceylon, mainly among the poorer economic groups, during the past 20 years and of the somewhat meagre literature on the pattern of cardiac and vascular disease in the island suggests that the incidence of atheroselerosis in Ceylon is higher than has been thought and may not be dissimilar to that in Great Britain. A small dietary survey carried out by the authors on middle-class subjects (69 men and women medical students living in

University hostels) showed that while the average caloric intake of this population was below that recommended by the Food and Agricultural Organization of the United Nations, the protein intake was satisfactory, supplying 13% of the total calories. The fat intake supplied about 25% of the caloric intake, but was poor in polyunsaturated fatty acids. The authors conclude that perhaps the high proportion of carbohydrates in the diet in combination with an insufficient intake of unsaturated fatty acids may be responsible for the significant incidence of atherosclerosis in Ceylon.

[This interesting paper is based on very little original work, but the available data are well utilized in the discussion and in comparing them with similar data accumulated in Western countries.]

Z. A. Leitner

860. What is Fallot's Tetralogy

H. R. S. HARLEY. American Heart Journal [Amer. Heart J.] 62, 729-734, Dec., 1961. 32 refs.

The essence of Fallot's tetralogy is the combination of a nonrestrictive ventricular septal defect with pulmonary stenosis of sufficient severity to impose a resistance to flow greater than that of the systemic peripheral vascular resistance. The nonrestrictive ventricular septal defect ensures that the pressure in the two ventricles is identical throughout the cardiac cycle under all conditions, and that their pressure is the same as that in the aorta throughout the ejection phase. The pulmonary stenosis reduces the pressure and flow in the pulmonary artery, and is responsible for a bidirectional or right-to-left shunt between the ventricles. Overriding of the aorta is quite variable in degree anatomically, and of little importance hemodynamically. Right ventricular hypertrophy is a nonspecific reaction to stress.

Fallot's tetralogy is defined as pulmonary stenosis with a bidirectional or reversed shunt through a nonrestrictive ventricular septal defect. The term Fallot's tetralogy is a misnomer. A more desirable eponymous title would be Fallot's anomaly.—[Author's summary.]

861. "Drop Attacks" in Cyanotic Congenital Heart-Disease

D. W. EVANS and O. Brenner. *Lancet* [Lancet] 2, 575-576, Sept. 9, 1961. 8 refs.

The authors of this paper from Queen Elizabeth Hospital, Birmingham, describe 3 patients with cyanotic congenital heart disease who had recurrent attacks of falling while walking. The onset of the "drop attacks" was sudden, although there might be some warning paraesthaesiae in the legs. The period of uselessness of the legs was very short and there were no epileptiform manifestations, although the electroencephalogram was abnormal in each case. The condition is likened to "akinetic" epilepsy and to the drop attacks of middle and old age.

A. I. Suchett-Kaye

DIAGNOSTIĆ METHODS

862. Combined Transthoracic Left and Percutaneous Right Heart Catheterization

P. KEZDI. Archives of Internal Medicine [Arch. intern. Med.] 108, 685-694, Nov., 1961. 10 figs., 15 refs.

From Chicago Wesley Memorial and Passavant Memorial Hospitals and Northwestern University Medical School the author describes his technique of simultaneous left and right heart catheterization. A polyethylene catheter, size PE50, is introduced through a thin-walled needle, gauge 18, into an antecubital vein and then fed into the right heart under constant monitoring of pressure. Left heart catheterization is performed by the Björk method and the Kent-Fisher modification with the patient in the prone position and under fluoroscopic control. The pulmonary artery was catheterized successfully in 90% and the left ventricle in 98% of 150 cases.

In cases of mitral stenosis a poor correlation was found between the diastolic mitral gradient and the calculated mitral valve area. In mitral insufficiency there was no close correlation between the rate of the "y" descent on the pressure pulse tracing and the degree of regurgitation as estimated by dye dilution studies (in which cardiogreen dye was injected into the left ventricle and blood samples were withdrawn through a second needle from the left atrium). In combined aortic stenosis and mitral stenosis there was a lower aortic gradient in relation to calculated aortic valve area than in pure aortic stenosis. This was due to the reduced cardiac output in the former condition, and there was a lower end-diastolic pressure, described as the "protective effect of mitral stenosis on the left ventricle in aortic stenosis". Left heart catheterization was useful in differentiating non-specific myocardial diseases with apical murmurs from mitral valvular disease. The complications encountered included haemothorax (4 cases), pneumothorax (8), haemoptysis (1), syncope (2), and atrial fibrillation (1).

K. G. Lowe

863. Differential Diagnosis of the Cardiovascular Diseases through Right and Left Heart Catheterization: a Review

A. A. LUISADA and J. SZATKOWSKI. Diseases of the Chest [Dis. Chest] 40, 572-589, Nov., 1961. 10 figs.

864. Marked Left Axis Deviation. Indication of Cardiac Abnormality

G. W. CURD JR., W. M. HICKS JR., and F. GYORKEY. American Heart Journal [Amer. Heart J.] 62, 462-469, Oct., 1961. 9 refs.

"Left axis deviation" is a common electrocardiographic diagnosis and is generally regarded as being of little significance. However, if the diagnosis is reserved for those cases showing a mean electrical axis between -30° and -90° it is usually found to be associated with some cardiac abnormality. Working at the Veterans Administration Hospital, Houston, Texas, the authors have reviewed the case records of 154 patients known to have had this degree of left axis deviation; all had come

to necropsy, and all were men. In only 4 cases was the heart clinically and anatomically normal. The commonest diagnoses in the remainder were cardiac infarction (52%), arteriosclerotic heart disease (13%), hypertensive heart disease (13%), and myocardial fibrosis without obvious coronary disease (8%). Emphysema, sometimes stated to be a cause of left axis deviation, was also frequent in this series, but never appeared to be the sole abnormality. A comparative analysis of 100 living patients with similar left axis deviation (but a higher mean age than the necropsied series) showed that 31 had a clinically normal heart. Again the largest pathological group was that of cardiac infarction (21%).

J. A. Cosh

865. The Two-catheter Technique in Indicator-dilution Cardiovascular Studies

E. G. DIMOND, A. BENCHIMOL, and E. W. CROW. British Heart Journal [Brit. Heart J.] 23, 621-631, Nov., 1961. 14 figs., 19 refs.

The authors describe from the Institute for Cardiopulmonary Diseases, La Jolla, California, their experience with a two-catheter technique in performing indicatordilution studies in 62 patients with congenital heart disease and 19 with acquired heart disease who ranged in age from one month to 55 years. The dye, cardiogreen, was injected through the first catheter and the blood sample was withdrawn by means of a pump through a cuvette attached to the second catheter, which had its tip upstream from the site of injection. For example, for a ventricular septal defect the injection was made into the main pulmonary artery and the sample was taken from the right ventricle. In all cases it was possible to detect and locate a left-to-right shunt "based on the early appearance curve just preceding the main venous curve". In some, instances the method detected left-toright shunts that were not diagnosed from the oxygen saturation of blood samples taken during catheterization. The technique was also used to detect valvular regurgitation; here the early appearance curve preceded the main curve by several seconds. C. T. Dollery

866. Time Relationships of the Left Atrial V Wave in Mitral Valvular Disease

P. G. F. NIXON. *British Heart Journal [Brit. Heart J.*] 23, 637-642, Nov., 1961. 4 figs., 20 refs.

Working at the General Infirmary at Leeds the author has examined the time relationship of the "v" wave recorded directly from the left atrium in 18 patients with rheumatic mitral valvular disease. He recorded phonocardiograms simultaneously from the mitral and pulmonary areas and pressures from the left atrium and the brachial artery.

The apex of the "v" wave occurred 0.01 to 0.04 second after closure of the aortic valve in 17 patients and 0.002 second before it in the remaining patient. The opening snap began 0.04 to 0.1 second after aortic valve closure and 0.04 to 0.1 second after the peak of the left atrial "v" wave. He suggests that the left atrial pressure is reduced before the mitral valve opens by active dilatation of the atrio-ventricular ring, and he

stresses the importance of interpreting correctly the first 0·1 second of the "y" descent, which may occur before the mitral valve opens. The series included 3 patients with mitral stenosis alone, 5 with mitral stenosis and regurgitation, and 5 with mitral regurgitation alone and the time relationship of the "v" wave peak to aortic closure proved to have no diagnostic value. The time interval of the second sound to the opening snap did not appear to be shorter in patients with mitral regurgitation in this series.

C. T. Dollery

867. Percutaneous Puncture of the Left Ventricle E. C. Brockenbrough, A. G. Morrow, J. Talbert, and E. Braunwald. British Heart Journal [Brit. Heart J.] 23, 643-648, Nov., 1961. 2 figs., 10 refs.

The authors report from the National-Heart Institute. Bethesda, Maryland, their experience of percutaneous left ventricular puncture on 226 occasions in 202 patients, of whom 79 had aortic stenosis, 66 mitral valve disease, and the remaining 57 had a variety of combined valvular acquired lesions or forms of congenital heart disease other than aortic stenosis. The procedure, which is fully described, was successful in 210 instances (93%) with no mortality, although significant complications developed in 14 studies. Pneumothorax occurred in 11 patients and there was also one case of cardiac tamponade and 2 of unexplained hypotension. The authors comment that the incidence of complications, although not high, is greater in their experience than with either the transbronchial or the transseptal route. They conclude that percutaneous puncture is a valuable alternative route if other methods fail and that it is particularly valuable in postoperative patients in whom obliteration of the pericardial and pleural sacs by adhesions lessens the risk of complications. C. T. Dollery

BACTERIAL ENDOCARDITIS

868. Subacute Bacterial Endocarditis at the University of Minnesota Hospital, 1939 through 1959

G. A. Pankey. Annals of Internal Medicine [Ann. intern. Med.] 55, 550-561, Oct. [received Dec.], 1961. 21 refs.

This review of 167 patients who had a bacterial infection of the endocardium of greater than 50 days' duration covers a period of 20 years, during part of which there was no effective therapy for subacute bacterial endocarditis. The author confirms that the condition usually has its onset in the third or fourth decade and that there is no difference in incidence between the sexes. The high incidence in earlier age groups in his own cases is attributed to the large number of young patients referred to the University of Minnesota Hospital, Minneapolis, for cardiac surgery.

Over half the cases had evidence of rheumatic heart disease, while congenital heart disease accounted for one-fifth. Infections of the upper respiratory tract, dental manipulations, and surgical operations, particularly transurethral resection of the prostate, were outstanding precipitating factors. The incidence of symp-

toms and signs was very similar to that in other reported series, and the organisms found on blood culture were α -haemolytic streptococcus, coagulase-negative staphylococci, and Streptococcus faecalis in descending order of frequency.

Of the 167 patients, 85 (51%) died in hospital or shortly after discharge. It was considered that 45% of patients with adequate follow-up were cured. A mortality of 84% in the years before the introduction of penicillin contrasts with a 39% cure rate in the subsequent years. The author notes no fall in mortality in the years following 1954, when larger doses of penicillin were beginning to be employed. Patients who developed subacute bacterial endocarditis in early life had a better prognosis than older patients.

At necropsy the mitral valve was found to be most frequently involved both in patients with valvular heart disease and those in whom no underlying heart disease had been detected in life. The commonest congenital defects were interventricular septal defect, tetralogy of Fallot, and patent ductus arteriosus. The neurological findings at necropsy showed that 25% had a suppurative encephalitis, and that subarachnoid or intracerebral haemorrhage, or both, occurred in 15%.

The author stresses that failure to culture the organism does not exclude subacute bacterial endocarditis. Sterile cultures were obtained in 17% of 182 attacks in the present series.

J. S. Malpas

869. Damage to the Aortic Valve as a Cause of Death in Bacterial Endocarditis

L. COHEN and L. R. FREEDMAN. Annals of Internal Medicine [Ann. intern. Med.] 55, 562-564, Oct. [received Dec.], 1961. 11 refs.

The authors report a study of the records of 33 cases of subacute bacterial endocarditis treated at Grace-New Haven Community Hospital, New Haven, Connecticut, "to call attention to a particular kind of valvular deformity, perforation or erosion of the aortic valve, as the most common cause of death from bacterial endocarditis" at that hospital during the past 5 years. Patients were considered to have recently damaged aortic valves when perforation or erosion was demonstrated at necropsy or changes in the character of the basal murmurs were noted while the patient was under observation.

Aortic insufficiency was present or developed in 15 of the 33 patients. Of the 13 patients who died, 7 had aortic valvular lesions. Thus the mortality rate in patients with aortic lesions was 54% compared with 28% in patients with lesions of other valves. This difference in mortality could not be attributed to failure of bacteriological cure, type of bacteria, age, or length of time between onset of symptoms and treatment. No correlation could be found between the degree of valvular damage and the type of infection; severe damage resulted even when the α -haemolytic streptococcus was the infecting organism.

It is noted that the poor prognosis of patients with an aortic valvular lesion complicated by subacute bacterial endocarditis has been apparent only since bacterial cure has become possible. It may therefore be necessary to consider repair of the valvular defect early as soon as bacteriological cure has been effected. J. S. Malpas

VALVULAR DISEASE

870. Arterial Embolization in Relation to Mitral Valvuloplasty

L. B. Ellis and D. E. Harken. American Heart Journal [Amer. Heart J.] 62, 611-620, Nov., 1961. 27 refs.

The authors of this paper from Harvard Medical School, Boston, Massachusetts, hold the view that in the natural history of mitral valve disease the danger of embolization increases with the severity of myocardial and valvular damage, the presence of atrial fibrillation, especially in patients over 40 years of age, and previous embolic incidents. It is their experience that valvulo-plasty with complete amputation of the appendage is prophylactic intervention well evidenced by their analysis of 1,500 cases so operated upon, the first 1,000 of which have already been reported (Circulation, 1959, 19, 803; Abstr. Wld Med., 1960, 27, 111).

Of the 1,500 patients, 260 had had one or more embolic incidents before being subjected to surgery, while 76 manifested this complication at operation and only 38 in the subsequent follow-up period. Embolism bore no relation to the presence or absence of thrombi on the atrial wall, but was twice as frequent in patients having had recent embolism within 8 weeks of operation and those with Group-III and Group-IV valvular disease.

While admitting that their experience with pre- and post-operative anticoagulant therapy has not been very extensive, the authors do not recommend the routine use of anticoagulants either early or late in the post-operative period, but emphasize the value of valvulo-plasty to avoid the hazards of recurrent embolization in patients with mitral stenosis even when symptoms are absent.

C. A. Jackson

871. Pulmonary and Revial Circulatory Adjustments to the Upright Posture in Patients with Mitral Valvular Disease

H. ELIASCH, H. LAGERLÖF, and L. WERKÖ. American Heart Journal [Amer. Heart J.] 62, 519-527, Oct., 1961. 3 figs., 32 refs.

This report from Karolinska Sjukhuset, Stockholm, and Sahlgren's Hospital, Göteborg, describes the orthostatic circulatory changes observed in 10 patients with mitral valvular disease. The patients were studied first in the recumbent posture and then tilted head-up to 45 to 60 degrees. The series included 3 patients with moderately elevated pulmonary arterial pressures, 4 with pulmonary pressures above 20 mm. Hg, and 2 with clinical signs of right heart failure. In all cases the cardiac output, pulmonary and systemic blood pressures, cardiopulmonary and total blood volumes, renal clearance of inulin and PAH, and the urinary excretion of sodium were determined.

In general the response to the change in posture was similar to that in healthy subjects, that is, a reduction in

cardiac and stroke output, a fall in pulmonary capillary and right atrial pressure, and also a fall in pulmonary arterial pressure and in both the pulmonary and systemic pulse pressures. There was a decrease in renal clearance of inulin and in the urinary excretion of sodium. In the 2 patients with clinical signs of right heart failure, however, the cardiac and stroke outputs remained unaltered although the pulmonary wedge pressure, the pulmonary arterial pressure, urinary sodium excretion, and renal clearance of inulin all showed a fall. This finding, it is suggested, could be due to the presence of sustained venomotor tone preventing the shift of blood to the lower part of the body. The 10th patient, who was not in heart failure or orthopnoeic, was studied in the headdown position (30 degrees from the horizontal); in this case no symptoms appeared and no major haemodynamic change was recorded.

The patients in this study had fewer respiratory difficulties in the upright position than in the horizontal. On the other hand one patient with mitral stenosis could be tilted head down and kept in this position for 30 minutes without discomfort. The question whether the respiratory symptoms in the horizontal position depend upon the increased blood volume in the lungs or upon the increased capillary pressure with increased exudation cannot be answered, since both blood volume and capillary pressure varied in the same direction. Probably both give rise to sensations that are of importance for the symptom of orthopnoea.

G. Clayton

CORONARY DISEASE AND MYOCARDIAL INFARCTION

872. Coronary Heart Disease in London Busmen. A Progress Report with Particular Reference to Physique J. A. Heady, J. N. Morris, A. Kagan, and P. A. B. Raffle. British Journal of Preventive and Social Medicine [Brit. J. prev. soc. Med.] 15, 143-153, Oct., 1961. 2 figs., 16 refs.

In previous papers it has been shown that the death rate from coronary arterial disease (especially the incidence of sudden death) is greater in the men who drive than in those who conduct London's double-decker trams, buses, and trolley-buses; it has also been shown that the drivers take larger uniforms than the conductors, and this suggested that the drivers were of different physique, even initially. In an attempt to decide whether this initial difference accounted for the different mortality from coronary arterial disease or whether the actual work was responsible the authors carried out further studies on the same group of workers.

Study covering a 4-year period showed that, among men aged 35 to 64, drivers were more liable to first attacks of angina pectoris or myocardial infarction, and especially of myocardial infarction which caused death within 3 days ("sudden death"). Over a 10-year period, representing 200,000 man-years, drivers under 50 were 3 times more liable to "sudden death" from coronary arterial disease than conductors under 50, and drivers over 50 were 50% more liable than conductors of the

same age group. Waist and chest girth tended to increase with age in both occupations; but in every age group the girth of drivers exceeded that of conductors, and this difference was not accounted for by increased height.

Clinical measurements were made to test the validity of the use of uniform sizes in such a study. Girth, measured clinically, correlated very well with the size of uniforms; there was, for example, no tendency to issue the drivers with more loosely fitting uniforms. Conductors were thinner for their height and had thinner skin-folds (that is, less fat) than drivers. Measurements of trousers and jackets showed that drivers who had begun work as conductors were intermediate in girth between conductors and men who had joined the company as trained drivers of heavy vehicles.

To obtain direct evidence of the relationship of girth or fatness to coronary arterial disease, clinical measurements of men with coronary arterial disease were compared with those of controls matched for age, occupation, length of service, and place of work, but no significant difference was found, except that skin-folds were thicker in affected conductors than in controls. (Unfortunately, these measurements were taken 1 to 6 months after the occurrence of coronary arterial disease and must exclude men who died suddenly.) When the men were divided into 6 groups—3 trouser-waist sizes each for those over 50 and under 50—there was a clear excess of sudden deaths from coronary arterial disease in drivers compared with conductors in all 6 groups.

It is concluded: (1) that conductors are less liable than drivers to develop coronary arterial disease, and in particular to die suddenly from it; (2) they are less stout than drivers at all ages; (3) there is no clear relationship between physique and the chance of developing coronary arterial disease or dying from it; and (4) the differences between conductors and drivers cannot be explained on the basis of physique alone and must also be due to the differences in work performed.

T. B. Begg

873. Anticoagulant Treatment in Acute Coronary Occlusion with "So-called" Ischemic Pattern

J. EDEIKEN. Diseases of the Chest [Dis. Chest] 40, 439-447, Oct., 1961. 7 figs., 12 refs.

Russek and Zohman (J. Amer. med. Ass., 1957, 163, 922; Abstr. Wld Med., 1957, 22, 201) defined criteria for the recognition of mild "good-risk" cases of myocardial infarction. Without anticoagulants, prognosis was good in these cases and there was a low incidence of thromboembolic complications and of further infarctions.

The author of this paper from the Hospital of the University of Pennsylvania, Philadelphia, points out the impossibility of determining, early in the illness, what the subsequent course of the individual patient may be, even though the outlook for "good-risk" cases as a whole may be good. From a total of 200 patients, 22 were selected who could initially be categorized as "good risks". Their clinical history strongly suggested a recent infarction, but the electrocardiographic changes were those of "ischaemia", that is, T-wave inversion with S-T depression in some cases. All had a recurrence of cardiac pain after an interval varying between

a few days and a few weeks, accompanied this time by classic cardiographic signs of infarction with Q waves. Of the 22,.18 were not given anticoagulants, or had not had such treatment for a long enough time to be effective; of these, 5 died. Of the remaining 4, who were treated effectively with anticoagulants, 2 died.

Thus in an initially mild case there may be an unpredictably severe recurrence or extension of infarction. Anticoagulants may not prevent this, and the recurrence may be fatal, but the author feels that the administration of anticoagulants is justified in the hope of preventing pulmonary or systemic embolism.

J. A. Cosh

874. The Relation between Arterial Pressure and Angina Pectoris. (Les relations de la tension artérielle et de l'angor coronarien)

A. JOUVE, J. L. MEDVEDOWSKY, R. BENYAMINE, and G. RENNER. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 37, 2963–2968, Nov. 2, 1961. 3 figs., 15 refs.

The authors report from Marseilles an investigation of the relationship between arterial hypertension and angina pectoris. The first part of the study concerned the role played by heredity, personality characteristics, physical build, and the blood levels of cholesterol, sugar, and uric acid and blood pressure in patients suffering from angina pectoris, while the second part was devoted to an attempt to ascertain the importance of the above mentioned factors in cases of angina pectoris without hypertension, in cases of essential hypertension without cardiac pain, and finally in cases of angina pectoris associated with hypertension. The third part consisted of a comparative study of complications normally seen in hypertension (with special reference to fundal changes and left ventricular hypertrophy) and correlation of the degree of severity of the arterial pressure with the presence of cardiac pain.

The authors could find no causative link between angina pectoris and elevation of the blood pressure. In only about one-quarter of the 225 patients included in this study was the blood pressure 180/100 mm. Hg or greater. In comparison, 71% of these patients were considered to have an "obsessional personality" and 79% as being of the "android" somatotype. It is concluded that both angina pectoris and high arterial pressure are parallel manifestations of a wider arterial disorder in man.

A. I. Suchett-Kaye

875. Functional Coronary Insufficiency—Anatomo-physiological Aspects and Criteria of Clinical Diagnosis. (L'insuffisance coronarienne fonctionnelle—abord anatomo-physiologique et critères de diagnostic clinique) R. FROMENT, J. LENÈGRE, A. PERRIN, J. HIMBERT, and J. NORMAND. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 37, 3327–3335, Dec. 2, 1961. Bibliography.

This paper from the Hôpital Boucicaut, Paris, and the Hôpital Edouard Herriot, Lyons, is based on a joint series of 1,828 cardiac patients who were followed up and finally came to necropsy in the years 1949-59. Functional coronary insufficiency was diagnosed in 50 (11.7%) of 427 patients with angina of effort and in 38 (8%) of 472 patients with myocardial infarction. The diagnosis of functional coronary insufficiency was made

in the presence of a typical symptomatology and in the absence of any anatomical evidence of coronary occlusion. Electrocardiograms were helpful in only 40% of cases. The following were thought to account for the 50 cases of functional coronary insufficiency among the 427 patients with angina of effort: aortic stenosis in 21 (4.9% of the total); aortic insufficiency in 2; anaemia in 3; repeated pulmonary emboli in 2; and bradycardia with atrioventricular block in 2; while less certain causes were hypertension in 10 patients and such causes as primary pulmonary hypertension, pulmonary stenosis, and paroxysmal tachycardias in the remaining 10. Among the 472 patients with myocardial infarction there were 4 cases of aortic stenosis, 6 of pulmonary embolism, 4 of recurrent paroxysmal tachycardia, and 2 of peripheral collapse following haemorrhage; in 22 cases gross cardiac enlargement was considered to be the main cause of functional coronary insufficiency. The authors discuss the role of tight mitral stenosis, but believe that this is a rare cause of functional coronary insufficiency, since in another series of 201 cases it was found in only 3.5%.

A. J. Karlish

876. Myocardial Infarction Treated by Early Ambulation. Effect of Prolonged Anticoagulant Therapy on the Immediate Prognosis after Discharge from Hospital P. Brummer, E. Linko, and V. Kallio. American Heart Journal [Amer. Heart J.] 62, 478-480, Oct., 1961. 2 refs.

In a previous report (Amer. Heart J., 1956, 52, 269) the authors described the effects of early ambulation and discharge from hospital in 236 out of 332 cases of cardiac infarction admitted to Turku University Medical Clinic, Finland, during the period 1952-4. In general, patients were allowed out of bed after 2 weeks and were discharged home a week later, anticoagulant drugs being given only while they were in hospital. They now review 321 out of 565 patients admitted in the period 1957-9 who were treated similarly, but continued taking anticoagulant drugs at home. The two series each covered a period of about 24 years, thus seeming to imply that the incidence of cardiac infarction had increased by about 70%. The later series contained a lower proportion of women (18% against 29%), but otherwise the two series were comparable.

In the first 2 weeks of treatment, that is, while still in bed, 22.5% of the later series died (22.4% in the earlier). In the third week, while the patients were ambulant, there were 4 major complications in the later series (one sudden death, 2 new infarctions, and one case of severe heart failure, ultimately fatal) compared with 3 in the earlier series. In the month after discharge there were 16 major complications in the later series (8 new infarcts of which 2 were fatal, and 8 readmissions with chest pain) compared with 30 in the earlier series (one sudden death, 21 new infarcts, and 8 readmissions with chest pain). The significant difference in the immediate postdischarge course suggests a protective effect from the continued anticoagulant therapy. [One month is a short time to judge this issue, and a longer follow-up is really, needed.] The safety of allowing ambulation after 2 weeks is, however, confirmed. J. A. Cosh

PULMONARY CIRCULATION -

877. The Late Appearance of Leg Symptoms in Pulmonary Embolus

A. E. STEVENS. Lancet [Lancet] 2, 1005-1007, Nov. 4, 1961. 10 refs.

From a series of 117 consecutive cases of pulmonary infarction seen at the Canadian Red Cross Memorial Hospital, Taplow, the author selected 14 patients in whom the chest symptoms preceded any evidence of venous thrombosis, including one in whom no leg symptoms ever developed. Of these patients, 8 were apparently well and active at the onset of their symptoms and in 9 cases the illness simulated pneumonia and was treated as such. It seems that clinically diseased leg veins, whatever their state of chronicity, should, in the presence of equivocal chest symptoms, be regarded as a potential source of emboli. Patients who are active but have atypical pneumonic symptoms and apparently normal veins should always be observed with the possibility of pulmonary infarction in mind. Haemoptysis in such a patient is particularly suggestive. The author states that although these conclusions are based largely on clinical opinion, they are presented since it is important that pulmonary infarction should not be misdiagnosed and so lead to a delay in beginning treatment with anti-Leon Gillis coagulant drugs.

878. A Triad for the Diagnosis of Pulmonary Embolism and Infarction

W. E. C. WACKER, M. ROSENTHAL, P. J. SNODGRASS, and E. AMADOR. *Journal of the American Medical Association* [J. Amer. med. Ass.] 178, 8-13, Oct. 7, 1961. 2 figs., 17 refs.

It has been stated that the diagnostic accuracy of pulmonary embolism by clinical, radiographic, and electrocardiographic criteria alone varies from only 20 to 50%. In this paper from the Peter Bent Brigham Hospital, Boston, the authors describe a new method for the diagnosis of pulmonary embolism and infarction, namely, the simultaneous serial measurement of serum lactic dehydrogenase (L.D.H.) activity, serum glutamicoxalacetic transaminase (G.O.T.) activity, and serum bilirubin concentration. In a series of 17 patients with pulmonary embolism or infarction, the serum L.D.H. level was consistently elevated and the serum G.O.T. activity consistently normal, while the serum bilirubin level was increased in 12 patients. This triad of results in the diagnosis of pulmonary embolism and infarction occurs early in the course of the disease and helps to differentiate the condition from myocardial infarction and pulmonary infection. It is noted, however, that in patients with severe liver disease this diagnostic method is often useless because of the already abnormal values for serum L.D.H. and G.O.T. activity and bilirubin

[The three laboratory tests mentioned above, if performed within 2 days of the onset of symptoms, will become standard procedure for the investigation of patients suspected of pulmonary embolism and infarction.]

A. I. Suchett-Kaye

Clinical Haematology

879. Hypoplastic Anaemia Treated by Transfusion of Foetal Haemopoletic Cells

R. Bodley Scott, J. Q. Matthias, M. Constandoulakis, H. E. M. Kay, P. F. Lucas, and J. D. Whiteside. British Medical Journal [Brit. med. J.] 2, 1385–1388, Nov. 25, 1961. 4 figs., 13 refs.

In this paper are reported 14 patients with a variety of forms of marrow aplasia who have been treated with stored or fresh foetal liver cells. Two of the cases in which a diagnosis of leukaemia was ultimately made are excluded because it is unlikely that marrow dysfunction would be corrected by simple injection of foetal liver cells. Four of the patients were children, and 2 of these had a disease probably congenital in origin; all had different types of aplasia. The 8 remaining cases, in adults, consisted of 4 with acute and 4 with chronic pancytopenia. Most of these patients did not respond to treatment and there were a number of early deaths. In only 2 cases has a remission occurred, and these are described in detail. In one, a case of chronic hypoplastic pancytopenia, there was a minor reticulocyte response after the first injection of foetal liver and the subsequent transfusion requirements fell markedly, but there was some evidence that the transfusion requirements had been gradually decreasing before the foetal liver was given. The patient later had 3 further injections of foetal liver, with a more marked reticulocyte response and what appeared to be a more obvious response to the treatment. His transfusion requirements have fallen still further, and only 4 pints (2.3 l.) of blood has been required in the last year. In this case there may have been slow but spontaneous recovery, but the fact that there was a reticulocyte response after the injection of foetal cells and no further improvement until another injection of foetal cells was given suggests that the response was due to the foetal cells. The second patient, who also had chronic hypoplastic pancytopenia, received 4 injections of foetal liver at the outset. There was no reticulocyte response, but there was an increase in platelet and leucocyte counts which was maintained. The transfusion requirements did not fall immediately, but for one year after the injections they were not increased and for a further year no more transfusions have been given. The lack of data from which the rate of haemoglobin decline in the early stages of the disease could be calculated makes it difficult to assess the effect of treatment in this case; it is suggested that the recovery was in all probability spontaneous and not related to the liver injections.

The authors state that although 2 of their 14 patients, both with chronic pancytopenia, have had a remission following the injection of foetal cells, the true value of these observations is difficult to assess, as it seems likely from recent reviews that a little under one-third of such cases may recover spontaneously. Neither of the 2

patients showed any evidence of chimerism, while it is not possible to state that the foetal cells themselves were established in the recipient. It is possible, however, that a temporary proliferation of foreign cells may help the impaired cells of the patient to recover or that some direct humoral factor is involved.

R. F. Jennison

880. Syndrome of Iron Deficiency Anemia, Hepatosplenomegaly, Hypogonadism, Dwarfism and Geophagia A. S. Prasad, J. A. Halsted, and M. Nadimi. American Journal of Medicine [Amer. J. Med.] 31, 532-546, Oct., 1961. 3 figs., 15 refs.

The authors describe an unusual syndrome observed at the Saadi and Nemazee Hospitals, Shiraz Medical Center (University of Shiraz Medical School), Iran. This syndrome consists in severe iron-deficiency anaemia associated with some degree of hypogonadism and dwarfism and is also associated with enlargement of the liver and spleen. All the patients were males and suffered from malnutrition. There were 11 patients in the series and nearly all had the unusual habit of eating clay or charcoal which is termed geophagia.

The anaemia was not associated with blood loss or malabsorption and responded adequately to oral iron. The diet contained adequate amounts of iron, but it was considered that the predominantly wheat diet with its high phosphate content interfered with absorption. Treatment was highly successful in curing the anaemia and reducing the size of the liver and spleen, and there is some indication that the endocrine change was reversible. The cases are described in detail and the syndrome appears to be common in Iran.

[I. MeLean Baird]

881. Studies Suggesting the Presence of Intrinsic Factor in Bile

V. HERBERT and M. E. KAPLAN. Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol. (N.Y.)] 107, 900-904, Aug.—Sept. [received Nov.], 1961. 1 fig., 22 refs.

Experiments carried out at the Thorndike Memorial Laboratory, Harvard Medical School, provided evidence that there is present in human bile and, to a lesser extent, in rat bile a substance which shows intrinsic-factor activity. This material gave a "reaction of identity" with concentrates of intrinsic factor from hogs, rats, and human subjects when subjected to Ouchterlony agar double diffusion analysis, and also enhanced the uptake of labelled vitamin B₁₂ by rat liver homogenates. However, Schilling tests for the uptake of vitamin B12 performed on 2 patients with pernicious anaemia and one who had been subjected to total gastrectomy failed to show any increased absorption of the vitamin when 200 ml. of human bile was added. The authors point out that the amount of intrinsic-factor-like material in bile is small and, even if it be proven to be true intrinsic factor, . . enhancement of B₁₂ absorption. Specimens of rat bile gave inconstant positive results when tested for an enhancing effect on absorption of the vitamin in a gastrectomized rat and in everted sacs of rat small intestine. They conclude that "it is possible that an enterohepatic circulation of intrinsic factor exists as a further phase of its activity with relation to Vit. B₁₂".

R. B. Thompson

882. Haemophilia Syndromes: a Survey of 267 Patients J. F. WILKINSON, F. NOUR-ELDIN, M. C. G. ISRAELS, and K. E. BARRETT. Lancet [Lancet] 2, 947-950, Oct. 28, 1961. 15 refs.

The authors describe the clinical and laboratory findings in 267 patients with either haemophilia or Christmas disease seen over a period of 25 years at the Royal. Infirmary, Manchester. The incidence of haemophilia (84.1%) relative to that of Christmas disease (15.9%) was similar to the ratio found by other workers in the United Kingdom. In most cases (231) the diagnosis was first made before the age of 5 years, but in 10 cases the disease was not diagnosed until after the age of 20. The most frequent first signs were excessive traumatic bleeding, haemarthrosis, spontaneous bruising and haematomata, bleeding from gums, epistaxis, and haematuria; and the most dangerous incidents were gastrointestinal bleeding and cerebral haemorrhage. Almost half the patients had required blood transfusion subsequent to tooth extraction. The blood-group distribution did not differ significantly from normal, and 114 patients had a normal whole-blood coagulation time. In no case, however, was there a normal response to the thromboplastin generation test. Clinical severity was correlated with the results of antihaemophilic globulin (A.H.G.) assay; an A.H.G. level of only 1% of normal was likely to be associated with a mild clinical gradation of severity.

The prognosis was found to be better than might be anticipated, there being only 20 deaths among the 267 A. S. Douglas

883. "Infraclinical" Forms of Lymphatic Leukaemia Localized Entirely in the Bone Marrow. (Les formes "infracliniques" à localisation médullaire pure des leucoses lymphoides chroniques)

J. OLMER, M. MONGIN, and R. MURATORE. Presse _médicale [Presse méd.] 69, 2051-2053, Nov. 4, 1961. 18 refs.

From the Faculty of Medicine, Marseilles, comes this report of 7 cases of chronic lymphatic leukaemia which was apparently restricted to the bone marrow. All 7 patients were females over the age of 50 years, 4 being over 70. The diagnosis was made either following a complaint of the symptoms of anaemia or as the result of haematological investigation in the absence of a complaint.

Only one patient had palpable splenic enlargement and in none was there lymphadenopathy. The degree of anaemia was slight. The leucocyte counts ranged from a normal level to 122,000 per c.mm., with small lympho-

it might require as much as a litre of bile to produce any cytes predominating; the platelet counts were within normal limits. In all cases the number of lymphocytes in the bone marrow was greatly increased. The serum protein level was within normal limits and showed no increase in that of globulin, so that a diagnosis of Waldenström's macroglobulinaemia was rejected. These patients have been observed for varying periods ranging from 11 years to a few months, but only 2 have been thought to require treatment. It is suggested that these cases are examples of a particularly benign form of chronic lymphatic leukaemia, which is likely to be diagnosed only relatively infrequently. A. G. Baikie

> 884. A Syndrome Resembling Adrenal Cortical Insufficiency Associated with Long Term Busulfan (Myleran) Therapy

> R. A. KYLE, R. S. SCHWARTZ, H. L. OLINER, and W. Dameshek. Blood [Blood] 18, 497-510, Nov., 1961. 1 fig., bibliography.

The occurrence of bone-marrow depression is the most significant complication of treatment with busulphan ("myleran"), but amenorrhoea, hyperpigmentation of the skin, gastro-intestinal reactions, hyperuricaemia with renal calculus formation, testicular atrophy, gynaecomastia, and interstitial pulmonary fibrosis have also been reported. The authors now report from Pratt Clinic-New England Center Hospital, Boston, 4 leukaemic patients on long-term busulphan therapy who developed hyperpigmentation of the skin, severe weakness. fatigue, anorexia, nausea, and loss of weight. Three of the patients were in haematological remission when the syndrome developed, while the fourth was in a blast crisis. The pigmentation was brownish in colour and generalized, but it did not usually involve the buccal mucous membrane, palmar creases, or scars. It was proved to be caused by melanin. Other causes of pigmentation, such as vitamin deficiency, arsenical poisoning, Hodgkin's disease, pernicious anaemia, Whipple's disease, cirrhosis of the liver, and scleroderma, were excluded. The weakness was enough to confine the patients to bed. The loss of weight varied from 15 to 58 lb. (6.8 to 26.3 kg.), and the anorexia was characterized by a distaste for meat.

Adrenal cortical insufficiency was suggested by the pigmentation, weakness and gastro-intestinal symptoms, though no evidence of its existence was obtained from estimation of the 17-ketosteroid and 17-hydroxycorticosteroid excretion or after ACTH stimulation. There was no response to cortisone, 25 mg. daily, or prednisone, 100 mg. daily, in the 2 cases in which these were tried. Variable successes attended the withdrawal of busulphan. Because busulphan is known to inhibit sulphydryl groups, a course of methionine was given to one patient, but with no apparent effect.

The authors suggest that, although the complete syndrome usually occurs after one to 5 years' administration of the drug, it is advisable to administer only enough busulphan as is necessary to keep the leukaemia under

[A good list of references to the literature on busulphan is given.] J. S. Malpas

Respiratory System

885. Ventilation Studies in Nonsmokers and Smokers G. Bower. Diseases of the Chest [Dis. Chest] 40, 386-390, Oct., 1961. 3 figs., 11 refs.

At the University of Colorado Medical School, Denver, the effect of cigarette smoking on air flow from the lungs was investigated by comparing the maximum midexpiratory flow rate (M.M.F.) in two defined groups of cigarette smokers and corresponding groups of nonsmokers. The M.M.F. is the mean flow rate (in litres per second) measured from the middle half of a tracing of a forced expiration, and in this study the maximum value from a set of three acceptable tracings was used; the author also calculated the maximum breathing capacity (M.B.C.) indirectly from the one-second forced expiratory volume, measured from the same tracings, by multiplying it by a factor of 40. Three groups of subjects were studied: (1) 98 healthy medical students, physicians, or hospital employees aged between 20 and 29 years, of whom 49 had never smoked, 18 had smoked 20 cigarettes (" one pack ") daily for less than 5 years, and 31 had smoked this amount for more than 5 years. (2) Eighty-four male bank employees, all aged over 40 and many of whom had cough, sputum, and exertional dyspnoea; these included 14 non-smokers, 17 who had smoked less than 20 pack-years, and 53 who had smoked 20 or more pack-years. (3) Seventy-eight female bank employees also all over 40 years of age who were subdivided as above into groups of 39; 17, and 22 respec-

In Group 2 there was a statistically significant difference between both the M.M.F. and the indirect M.B.C. of smokers in both groups and the non-smokers. In the younger subjects in Group 1 there was a significant difference between the M.M.F. of smokers of more than 5 pack-years and of smokers of less than 5 pack-years and of non-smokers, but that between smokers of less than 5 pack-years and non-smokers was not significant. The author concludes from these findings that changes in the airways occur within a short time of men starting to smoke. However, there was no significant difference between any of the sub-groups for either M.M.F. or M.B.C. in the female Group 3 which, he considers, suggests that women may react differently to tobacco smoke P. Hugh-Jones from men.

886. Prognosis of Intrathoracic Sarcoidosis in England: a Review of 136 Cases after Five Years' Observation J. G. SCADDING. British Medical Journal [Brit. med. J.] 2, 1165–1172, Nov. 4, 1961. 15 refs.

The author reviews 136 cases of pulmonary sarcoidosis which he has observed for 5 years out of 230 cases previously reported on (*Brit. med. J.*, 1960, 2, 1617; *Abstr. Wld Med.*, 1961, 29, 366). Clear chest radiographs have been achieved in 27 (84%) of 32 patients with hilar lymphadenopathy only, in 23 (53%) of 40 patients with

hilar lymphadenopathy and pulmonary shadowing, and in 16 (43%) of 37 patients with pulmonary shadowing but no hilar lymph-node enlargement. Of the remaining 27 cases, in which fibrosis was judged to be already present, improvement was obtained in only 7. Erythema nodosum was associated with a good prognosis, but other skin lesions with a poor one. Sarcoidosis of the eye, lymph nodes, and spleen did not seem to affect the prognosis of the lung changes in this series. During the period of observation 12 pregnancies occurred in 10 patients; lung mottling cleared during 4 of these pregnancies, only to recur after delivery.

D. Geraint James

887. Pneumocystis Pneumonia: Report of Three Cases in Adults and One in a Child with a Discussion of the Radiological Appearances and Predisposing Factors W. F. White, H. M. Saxton, and I. M. P. Dawson. British Medical Journal [Brit. med. J.] 2, 1327-1331, Nov. 18, 1961. 6 figs., 45 refs.

Pneumocystis pneumonia was found in 3 adults and one child aged $2\frac{1}{2}$ years. The adults had histologically proved and the child clinical evidence of primary malignant disease of lymphoid tissue. All had received long-term corticosteroid and antibiotic therapy; the adults had also had cytotoxic drugs and radiotherapy.

Review of these cases suggests that *Pneumocystls* pneumonia should be considered when cyanosis and breathlessness are out of proportion to physical signs, or when unexplained pulmonary consolidation is present in the later stages of reticulosis. A consideration of treatment received suggests that long-term corticosteroid therapy predisposed to the condition, and review of the experimental literature supported this view. There is some evidence that in children the disease may present in two forms, depending on the general resistance, and that poor resistance may sometimes be linked with low gammaglobulin levels.—[Authors' summary.]

888. Primary Lymphosarcoma of the Lung M. B. Kress and O. C. Brantigan. Annals of Internal Medicine [Ann. Intern. Med.] 55, 582-597, Oct. [received Dec.], 1961. 13 figs., 45 refs.

The authors present from Eudowood Sanatorium, Towson, Maryland, detailed case reports of 7 patients who were found to have primary lymphosarcoma of the lung; in all cases the tumour was either confined to the lung or there was convincing evidence that it originated as a primary tumour there. Since it is a rare condition (the authors state that only 51 cases have previously been reported) it may seem surprising that 7 cases have been collected, but this could be due to misdiagnosis of the cell type of the tumour. In this series one patient was diagnosed as having small-cell [oat-cell] carcinoma, but this conclusion was reconsidered and the histological

material re-examined when the patient was found to be the concept of any causal correlation between the two surviving a surprisingly long time. The favourable conditions, but suggest rather that chronic inflammation prognosis in primary lung lymphosarcoma [as in lymphosarcoma of the intestine]; compared with generalized lead to metaplasia with consequent malignant degeneralymphosarcoma or with oat-cell carcinoma, is very

The authors comment that a sarcoid reaction in lymph nodes draining the tumour area (without tumour deposits in the nodes), which may occur both in lymphosarcoma and in other malignant states, can make the differential - diagnosis difficult. Primary lymphosarcoma of the lung is most commonly observed in middle age, and affects both sexes with about equal frequency. The tumour is seen as a white, pale yellow, or greyish-pink mass with no capsule: it may produce few symptoms for some long while and frequently appears as a diffuse lesion in the chest radiograph.

The authors consider that resection is the treatment of choice for localized lesions, but that radiotherapy may be useful in addition to surgery or when operation is impracticable. They urge the necessity of considering the diagnosis of primary lymphosarcoma in studying pulmonary lesions if fewer cases are to be missed and more effective treatment given.

P. Hugh-Jones

889. The Development of Cancer of the Lung and Its Interrelationship with Tuberculosis. (Die Entwicklung des Lungenkrebses und seine Wechselbeziehung zur Tuberkulose)

A. E. RABUCHIN. Zeitschrift für Tuberkulose [Z. Tuberk.] 117, 281-294, 1961. 17 figs., 11 refs.

This paper from the Tuberculosis Department of the Central Institute for Post-Graduate Medical Studies, Moscow, discusses the problem of an association between - bronchial carcinoma and pulmonary tuberculosis. - In his clinical investigation the author studied 180 patients, of whom 61 had peripheral bronchial carcinoma and the remaining 119 tuberculosis. A review of the extensive literature and the results of his own studies have failed to show a convincing causal relationship between the two conditions, A. J. Karlish

890. Bronchial Carcinoma as a Sequel to Chronic Progressive Pulmonary Tuberculosis. (Das Bronchialkarzinom im Gefolge der chronisch fortschreitenden Lungentuberkulose)

H. BODENSTAB and W. QUARZ. Zeitschrift für Tuber-kulose [Z. Tuberk.] 117, 295–298, 1961. 3 figs., 21 refs.

There is an extensive literature linking bronchial carcinoma with pulmonary tuberculosis. In most reported cases the tuberculous lesions are healed and it has been generally assumed that the tuberculous scars, particularly those resulting from bronchial perforation by caseous nodes, are the site of developing carcinoma. It is of interest, therefore, that the 3 patients described in this paper from the Marienheide Hospital, Schömberg, Rheinland, all had active disease with tuberculous ulceration of the bronchus. In one case pre-cancerous epithelial changes and typical tubercles were noted in the same bronchial biopsy specimen. The authors reject

and continuous epithelial regeneration in the bronchi tion. A. J. Karlish

891. Panlobular and Centrilobular Emphysema: Correlation of Clinical Findings with Pathologic Patterns H. C. SWEET, J. P. WYATT, A. J. FRITSCH, and P. W KINSELLA. Annals of Internal Medicine [Ann. intern. Med.] 55, 565-581, Oct. [received Dec.], 1961. 6 figs.,

Using the technique of Leopold and Gough (Thorax. 1957, 12, 219 [not 14, 113 as given]; Abstr. Wld Med., 1958, 23, 317) for making paper-mounted entire lung sections, the authors working at St. Louis University School of Medicine, Missouri, have classified post mortem the lungs of 194 patients found to have emphysema into those showing centrilobular lesions, those with panlobular lesions, and those with both lesions. extent of the emphysema in all cases was estimated on the lung sections by a grid method and the patients then regrouped on the basis of their case records into those in whom (1) emphysema was the direct cause of death (43 cases); (2) emphysema contributed to the death (60 cases); (3) death was from another cause but symptoms due to emphysema were present during life (32 cases); and (4) death was from another cause and there were no symptoms from emphysema during life (59 cases).

The authors claim that they were able to differentiate the three types of emphysema, but that there was no clear-cut history, physical sign; or radiological or laboratory finding which definitely separated the types during life. However, they agree with other authors that a long history of chronic cough tends to go with the centrilobular type, and they also found that these patients tend to have an insidious onset of breathlessness and other symptoms, to be thin, to have small hearts and depressed diaphragms, and often to have bullae which are revealed radiologically. In contrast, they suggest that panlobular disease should be suspected in life if the patient is overweight, has a large heart, there is a relatively sudden onset of dyspnoea, and bullae are absent in the radiographs. On the average they found that 54% of the lung section area was emphysematous in the Group-1 cases (in which emphysema was considered to be the cause of death), 35% in Group 2 (in which emphysema contributed to death), and only 20% and 18% respectively in Groups 3 and 4 (in which it was only symptomatic or asymptomatic).

The authors do not state whether the clinical grouping was entirely independent of the pathological grouping. More important, the difficulty of obtaining control subjects with no emphysema in such studies makes the interpretation difficult. It may be that many of these findings (both clinical and those of pulmonary functional tests) occur in patients who have expiratory air-flow obstruction, for example, from bronchitis or asthma, but who show-no signs of emphysema post mortem.]

Urogenital System

892. Cycloserine in the Treatment of Infection of the Urinary Tract

J. Syme, J. D. Sleigh, J. E. Richardson, and J. McC. Murdoch. *British Journal of Urology [Brit. J. Urol.*] 33, 261–266, Sept., 1961. 3 figs., 8 refs.

/Cycloserine in a dosage of 250 mg. 8-hourly for 14 days was given at the City Hospital, Edinburgh, to 40 patients suffering from chronic urinary infections, most of which were due to Escherichia coli. In 9 of the patients there were anatomical abnormalities and 8 had diabetes mellitus. The clinical and bacteriological response was rapid in 36 patients, but a small proportion of these relapsed during the following 6 months. [Unfortunately not all the patients were included in the follow-up.] The levels of cycloserine in the blood and urine were estimated and the dosage of the drug was adjusted to the laboratory minimum inhibitory concentration. Plasma levels below 20 µg, per ml. were aimed at, which, in the authors' experience, are "unlikely to be associated with serious toxic effects", but 2 patients in the series had convulsions and one hallucinations. In 3 cases of infection due to Proteus vulgaris the results were not satisfactory. It is concluded that cycloserine is a valuable drug in the treatment of urinary infections which have failed to respond to the more commonly used drugs, particularly if the infection is due to Esch. coli. Arnold Pines

893. Cycloserine in the Treatment of Urinary Infection M. M. Kubik and K. Datta. British Journal of Urology [Brit. J. Urol.] 33, 267-270, Sept., 1961. 7 refs:

At Burton Road Hospital, Dudley, cycloserine was given in a dosage of 250 mg. 2 or 3 times a day for 7 days to 150 mainly elderly patients suffering from chronic urinary infections. In 76% of the cases infection was due to Escherichia coli and in 60% of these the urine became sterile. Patients with infection due to Proteus vulgaris and the paracolon bacillus did less well, the urine becoming sterile in 42%. Side-effects of the drug were minimal.

[Unfortunately there seems to have been no follow-up. It is surprising that catheter specimens were obtained from female patients. There are no details of any anatomical defects present.]

Arnold Pines

894. Intermittent Peritoneal Lavage

J. J. McCaughan Jr. and C. McGown. American Journal of Surgery [Amer. J. Surg.] 102, 519-523, Oct., 1961. 27 refs.

The authors report their 4 years' experience with intermittent peritoneal lavage at the Veterans Administration Hospital, Memphis, Tennessee. Peritoneal dialysis, although less efficient than the artificial kidney, has proved to be a simple and effective means of obtaining artificial renal dialysis, and it requires only a minimum

of equipment. Abdominal paracentesis is performed with a trocar through which a lavage catheter is introduced into the pelvic peritoneal cavity, 2,000 ml. of lavage solution in 1.5% dextrose being run into the abdomen under gravity over a period of 30 minutes. It is left in situ for about one hour and is then recovered (álso over 30 minutes) by lowering the original container to the floor. Since by means of peritoneal lavage it is possible to hydrate or dehydrate a patient it is therefore important that a strict record be kept of the intake and output both of the lavage fluid and other body fluids; the patient should be weighed daily. The correct placing of the lavage tube is of primary importance. Obstruction to the return of fluid may be due to fibrin. particles of fat, or the loculation of fluid by abdominal adhesions; raising the patient's head or changing his position will often produce a free flow of fluid. Heparin added to the lavage fluid impedes the formation of fibrin and helps to prevent blockage. The addition of amethocaine relieves any abdominal pain, while aqueous penicillin added to the solution lessens the chance of infection. As the lavage fluids now available commercially contain essentially balanced amounts of electrolytes to which the body fluids establish equilibrium, there is little danger of producing an abnormal electrolytic level in patients undergoing lavage. If it is desired to remove cedema fluid a hypertonic (7%) solution of dextrose may be used. Peritoneal lavage is contraindicated in patients with extensive abdominal adhesions or diffuse generalized peritonitis.

In the authors' series hyperpotassaemia, uraemia, and electrolyte abnormalities were present in all cases. Lavage was given for an average of 5.5 days and the volume of solution exchanged was 16,000 ml. per 24-hour period. During the first 24 hours of lavage the decrease in the blood urea nitrogen level averaged 56 mg. per 100 ml., and in potassium ion the average decrease was 1.6 mEq. per litre. Excellent palliation was achieved in most of the cases in spite of the poor prognosis. It is noted, however, that these patients with chronic renal conditions frequently die from the primary disease; often malignant, even though the lavage has corrected the abnormalities of the patient's blood.

J. M. Browne Kutschbach

895. Neurologic Complications of Acute Uremia S. Locke, J. P. Merrill, and H. R. Tyler. Archives of Internal Medicine [Arch. intern. Med.] 108, 519-530, Oct., 1961. Bibliography.

The neurological complications of acute uraemia were studied in 13 patients at the Peter Bent Brigham Hospital, Boston. Lassitude and lethargy passing rapidly into confusion, euphoria or depression, hallucinations, anxiety, and a sense of impending death were often noted and frequently alternated. The rate of alteration in the serum electrolyte levels, rather than the absolute levels,

was most closely connected with the symptomatology. Nystagmus, facial weakness, dysarthria, and variations in pupil size were frequent, fluctuating, and evanescent. Weakness, fasciculations, myoclonus, wasting of the muscles and sometimes stiff neck were present. The reflexes were always altered and varied rapidly. Sensory loss was not observed. At some time during the illness 5 of the patients had generalized convulsions; the varied changes in the electroencephalogram in these cases are described, but none of these changes could be correlated with the blood chemistry.

Arnold Pines

896. Kidney Size and Its Deviation from Normal in Acute Renal Fallure: a Roentgendiagnostic Study. [Monograph, in English]

H. Moëll. Acta radiologica [Acta radiol. (Stockh.)] Suppl. 206, 1-74, 1961. 33 figs., bibliography.

897. Alport's Syndrome of Hereditary Nephritis with Deafness

D. A. J. WILLIAMSON. *Lancet* [Lancet] 2, 1321-1323, Dec. 16, 1961. 4 figs., 27 refs.

This paper from the Southampton and Winchester Group Hospitals describes the features of a syndrome of hereditary nephritis associated with deafness occurring in 3 families and involving 14 individuals. Since it was Alport (*Brit. med. J.*, 1927, 1, 504) who first adequately described the main features of the condition the present author suggests that it should be referred to as "Alport's syndrome", at least until the aetiology is known.

In most subjects symptomless haematuria and proteinuria, with normal results of renal function tests, have been the first findings. In males the disease progresses to a chronic nephritis, with a fatal outcome before the age of 30. In contrast, females are rarely severely affected, and many have a normal life expectation in spite of intermittent or continuous proteinuria. Histological examination of the kidney in fatal cases reveals a chronic glomerulonephritis. Perceptive deafness is insidious in onset, but may become disabling; it occurs/more frequently in affected males. Occasional patients show associated ophthalmic abnormalities such as cataracts and spherophakia. (Full details of individual cases are given, together with figures to illustrate distribution in each family tree.) It is thought that the renal lesion is transmitted as a partially sex-linked dominant trait, but the mode of inheritance of the deafness is uncertain.

The author suggests that the syndrome may be less uncommon than is at present realized, since his cases accounted for "more than a quarter" of the individuals with acute nephritis who had abnormal urine at the sixmonthly follow-up examination.

Hewett A. Ellis

898. 164 Children with Nephrosis

G. C. Arneil. Lancet [Lancet] 2, 1103-1110, Nov. 18, 1961. 7 figs., 39 refs.

The author reviews and classifies according to the pathogenesis cases of the nephrotic syndrome occurring in children admitted to the Royal Hospital for Sick Children, Glasgow, between 1929 and 1957, and in the

present report describes 164 cases of "nephrosis", that is, in which there was "no obvious precipitating cause". Each case was followed up until 1959, the minimum period being 2 years, and so far 102 of these patients have survived.

No seasonal incidence of the condition was observed. The patients' ages ranged from below 6 months to 13 years, but only 4 cases occurred in the first 6 months of life, the peak incidence of onset (48 cases or 30%) being between the ages 7 and 18 months. Periorbital oedema was an early symptom in 156 cases (95%), and was present on admission in 162 (99%); ascites was noted in 77 (47%). In 53 cases (32%) there was a history of a preceding infection or fever and overt infection was present in 33 (20%) at the time of admission to hospital. Urinary protein excretion varied from 0.25 to 10 g. per day, mostly albumin. On admission macroscopic haematuria was noted in 18 (11%) and microscopic haematuria in 29 (18%), but in 135 (82%) there was no evidence of haematuria; Systemic hypertension occurred early in the disease in 10 children. The serum non-protein nitrogen level was normal (less than 45 mg. per 100 ml.) in 153 (95%) of 161 children tested, but was raised in 5 (28%) of the 18 with macroscopic haematuria and in 3 (2%) of the remaining 146 children. Electrophoretic examination of the serum proteins revealed the characteristic hypoalbuminaemia and it was observed that patients were usually oedematous when the serum albumin level was less than 1-g. per 100 ml.

Treatment before 1951 was variable and its results not consistently successful. Subsequently, however, these cases were treated with steroids and usually showed immediate improvement. Since the introduction of steroids the mortality and morbidity from infection and renal failure have diminished. The present regimen consists in the administration of a high-protein, low-salt diet, antibiotics, and prednisolone, this last being given initially in doses of 60 to 80 mg. per day, reduced over a 6-week period to 10 to 20 mg. per day, and continued in this dosage for 6 to 46 weeks; prednisolone is usually discontinued when proteinuria becomes slight (100 mg. per day) or ceases, but the dosage and duration of administration of the hormone are modified in individual patients who fail to respond satisfactorily or relapse. As stated above, of the 164 patients, 102 (62%) survived the study period and of these 80 (49%) were asymptomatic and 22 (13%) had residual proteinuria. In the 62 (38%) fatal cases 29 of the patients (18%) died from renal failure and 33 (20%) from infections. The prognosis was better in young female children; haematuria was an unfavourable feature.

The author concludes that the previously held gloomy outlook for this condition in children is now outmoded.

Hewett A. Ellis

899. Renal Papillary Necrosis: a Clinical Study of 103 Cases. [Monograph in English]

N. HULTENGREN. Acta chirurgica Scandinavica [Acta chir. scand.] Suppl. 277, 1–84, 1961. 19 figs., bibliography.

Endocrinology

900. Magnesium Metabolism in Parathyrold Disease S. Hanna, K. A. K. North, I. MacIntyre, and R. Fraser. British Medical Journal [Brit. med. J.] 2, 1253– 1256, Nov. 11, 1961. 6 figs., 12 refs.

In-this paper from the Postgraduate Medical School of London some biochemical findings in 7 cases of hyperparathyroidism treated by surgical removal of the gland are presented. In each of these cases the magnesium balance was negative before operation, though it is emphasized that this loss is not very great, nor is it a constant finding. Its cause is considered to be the competition between calcium and magnesium for a common transport resorption mechanism. The increased filtered load of calcium in the kidneys will lead to an increase in magnesium loss. After operation the balance always became positive, owing mainly to reduced urinary loss, the plasma magnesium level, which had previously been at or near the normal level, being reduced. This is because the increased bone resorption occurring before operation is corrected, while bone formation continues normally, with a resultant fall in extracellular magnesium level.

This postoperative hypomagnesaemia can be, controlled by oral supplements. It is important that these be given prophylactically to prevent the dangers associated with magnesium deficiency.

E. H. Johnson

901. Dynamics of Reparative Changes in the Bony Skeleton in Hyperparathyroid Dystrophy after Surgical Intervention. (Динамика репаративных изменений костного скелета в рентгеновском изоображении при гиперпаратиреоидной остеодистрофии после хирургического вме шательства)

B. M. IOFFE and M. I. SANTOCKIJ. Проблемы Эндокринологии и Гормонотерапии [Probl. Endokr. Gormonoter.] 7, 82-88, Nov.-Dec., 1961. 3 figs., 10 refs.

In this study 12 patients who had been treated surgically for hyperparathyroidism which had produced skeletal changes (cysts or osteoporosis) were followed up for periods ranging from 1 to 16 years. It was found that in all cases after removal of the parathyroid tumour bone structure was rapidly restored. At first the cysts were more evident radiologically, owing to thickening of their walls, but thereafter with the growth of bone the size of the cysts diminished until they disappeared. Fractures likewise underwent repair, and only deformities which had become established before the operation still persisted. Calcification in the kidneys, however, did not disappear.

The authors point out the importance of diagnosing the true condition before irreparable deformities occur. Thus in one of these cases a fractured cystic patella had been removed before the presence of a parathyroid tumour was discovered, and in another the cystic condition of the bones was treated by local radiotherapy. Renal calculi are an indication for careful radiological survey of the skeleton for the possible presence of osteo-dystrophia fibrosa cystica due to hypertrophy or adenoma of the parathyroid glands.

L. Firman-Edwards

PITUITARY GLAND

902. A New Type of Diabetes Insipidus Due to Increased Hormone Inactivation: Its Incidence in Clinical Material J. HANKISS, M. KESZTHELYI, and B. SIRO. American Journal of Medical Sciences [Amer. J. med. Sci.] 242, 605–611, Nov., 1961. 2 figs., 22 refs.

A new type of diabetes insipidus is described, in which the primary cause of the disease is ascribed to enhanced inactivation of the antidiuretic hormone [ADH]. Twenty-six patients with diabetes insipidus were thoroughly investigated by special tests, including the determination of the ADH-level of plasma and the *in vivo* pitressin-inactivation by the body. The response of the patients to pitressin therapy was also taken into consideration.

Nine cases were found in which the pitressin-inactivation test proved to be positive. These were, except for 2 instances of histiocytosis, all "idiopathic" cases. In the central type of diabetes insipidus, the hormone inactivation proved to be normal. In all but one case a primary cause responsible for the lesion of the anti-diuretic center could be found.

In the light of these findings, it is suggested that the primary cause of most "idiopathic" cases of diabetes insipidus is the increased inactivation of ADH (in the liver and kidneys), and that the hypothalamo-pituitary system becomes exhausted only at a later stage. Thus this type of diabetes insipidus belongs to the enzymopathic diseases.—[Authors' summary.]

903. Hypopituitarism Associated with Intracranial Aneurysms

W. VAN 'T HOFF, R. W. HORNABROOK, and V. MARKS. British Medical Journal [Brit. med. J.] 2, 1190–1194, Nov. 4, 1961. 2 figs., 38 refs.

This report from the Westminster Hospital and the National Hospital, Queen Square, London, describes 3 cases of pituitary dysfunction associated with intracranial aneurysms: The first was that of a woman aged 32 whose menstruation ceased at the age of 19. The sight of her left eye was poor 3 years later. Two years later still she became blind and was found to have oculomotor palsies, a large sella turcica, and a large left carotid aneurysm. The left common and internal carotid arteries were ligated, but she remained very ill for 2 years. At the end of this time she showed signs of hypopituitarism, the sella was even larger than before, urinary gonadotrophin excretion was low, and there was labora-

tory evidence of thyroid and adrenal cortical hypofunction. She improved greatly on treatment with thyroid, cortisone, and an androgen.

The second patient was a man aged 54 who presented with vertigo and vomiting. He was found to have mild diabetes mellitus as well as the appearance of hypopituitarism and destruction of the pituitary fossa. After treatment with tolbutamide for a few months his fasting blood sugar level was normal, but a glucose tolerance curve was diabetic in type. The response to insulin was delayed and prolonged. Adrenal cortical function was poor, but improved under treatment with ACTH (corticotrophin). There was a large right carotid aneurysm, but it was decided that surgical treatment was not justified.

The third patient, a woman aged 63, had had a subarachnoid haemorrhage 2 years before and had suffered from failing vision, headaches, and intolerance of cold for the past 6 months. Besides bitemporal hemianopia, the findings were those of thyroid and adrenal cortical hypofunction. There was an aneurysm in the region of the anterior communicating artery. This patient improved greatly following treatment with thyroid and cortisone.

Such cases as these are shown to be unusual. They are discussed in terms of interference with the blood supply of the hypothalamus.

G. C. R. Morris

904. The Development of the Human Hypophysis and Differentiation of its Anterior Lobe Cells in Embryonic Life. (Раввитие гипофива человека и дифференцировка клеток его передней доли в течение эмбриональной живни)

L. I. FALIN. Проблемы Эндокриноловии и Гормоноmepanuu [Probl. Endokr. Gormonoter] 7, 24—33, Nov.— Dec., 1961. 8 figs., 12 refs.

The author examined 23 human embryos of from 4 to 27 weeks in longitudinal sections (of the whole embryo in those up to 8 weeks, and of the head in the older ones). Various stains—haematoxylin-cosin, Heidenhain's azocarmine, resorcin-fuchsin, aldehyde-fuchsin, and Schiff's reagent after oxidation with periodate (the P.A.S. reaction)—were employed for differentiation of the anterior lobe cells.

At 4 weeks, Rathke's pouch passes up behind the forebrain as a narrow tubular pouch. The cells at this stage show no granules. By the fifth week the pouch is separated from the stomodeum, and the pouch is in close apposition to the infundibular recess and its outgrowthwhich forms the hypophysis. By the eighth week a plate of cartilage forms between the stomodeum and the pouch, which assumes an L-shaped form, the distal end becoming vertical to this plate, while the proximal part lies parallel to it. At this stage young β cells can be recognized by the P.A.S. reaction and resorcin-fuchsin. At the ninth or tenth week acidophil cells can be detected by their staining with azocarmine. The majority of the cells, however, are still indifferent to these stains, and only towards the end of the seventh month are the chromophil cells in the majority (the basophils predominating).

The conclusion is that differentiation takes place at an early stage of development; but is not complete until late in foetal life. The chromophibe cells are partly as yet undifferentiated chromophils and partly chromophils in a resting phase. The sella turcica, formed from the cartilaginous plate referred to above, can be seen housing the already formed pituitary body by the 20th week, but the gland does not fill it completely until the 27th week. Buds of epithelium can be seen growing from the walls of the hypophysial space into both anterior and posterior lobes during the third month of foetal life, while the space itself becomes gradually more and more obliterated by the growing anterior and posterior lobes between which it lies.

L. Firman-Edwards

905. The Measurement of the Hypophysial ACTH Reserve with SU 4885 (Metopyrene). (Die Bestimmung der hypophysären ACTH-Reserve mit SU 4885 (Metopiron))

H. KLEINFELDER, H. BRACHARZ, and E. GEBERT. Klinische Wochenschrift [Klin. Wschr.] 39, 1153-1159, Nov. 15, 1961. 5 figs., 34 refs.

The authors report from the University of Würzburg a comparative study of the pituitary ACTH reserve after the intravenous infusion of SU 4885 (metopyrone ditartrate) (given in a dosage of 30 mg. per kg. body weight in a solution of 500 ml. of isotonic sodium chloride solution with 2,000 units of heparin over 4 hours) as determined by three different methods: (1) assessment of the 24-hour urinary excretion of 17-ketogenic steroids by the method of Norymberski; (2) urinary excretion of 17-ketosteroids by Ruppert's modification; and (3) the urinary excretion of 11-deoxycorticosteroids (11-DOCS) by the method of Henke et al. In addition, the plasma 11-DOCS content was estimated before the infusion and 4 hours after it. The investigations were carried out on 5 normal men and 2 normal women. The best method appeared to be the estimation of 11-DOCS in the urine, since normally these steroids are not present either in the urine or in the plasma and are formed only as a result of the infusion of SU 4885.

In a further study of 6 patients (5 women and one man) with endocrine disorders, the pituitary ACTH reserve was shown to be completely eliminated in a woman whose acromegaly had been treated with implantation into the pituitary of radioactive yttrium and much reduced in a second similar case and also in a woman who had received daily treatment with 16 mg. of 6-methylprednisolone for 14 days. In a 4th female patient with a chromophobe adenoma the ACTH reserve was only slightly impaired. As might be expected SU 4885 is ineffective in Addison's disease, since here the adrenal cortex cannot respond to ACTH. An interesting finding was that in a 24-year old woman with idiopathic hirsuties, who showed an abnormal result although manifesting no signs of endocrine disorder, thus perhaps confirming the views of Kappas and collaborators, who considered that in such cases there is an excessive production of androgenic substances in an otherwise normal adrenal cortex.

[An interesting paper.]

THYROID GLAND

906. Thyroid Antibodies in Hypothyroidism. [In English]

B. SKANSE and S. B. NILSSON. Acta medica Scandinavica [Acta med. scand.] 170, 461-467, Oct., 1961. 3 figs., 16 refs.

It has been suggested that primary hypothyroidism may often represent the final stage of autoimmune thyroiditis. The present authors have investigated various types of hypothyroidism for thyroid antibodies, in the hope that this might help to clarify any immunological relationships in hypothyroidism. The clinical material consisted of 138 cases of hypothyroidism of varying origin and 54 patients who were euthyroid following treatment of thyrotoxicosis. The 138 hypothyroid cases comprised 60 cases of idiopathic and 38 of postoperative hypothyroidism, 15 cases following treatment with ¹³¹I, 15 due to chronic thyroiditis, and 10 patients with goitre of undefined type. The tests used to study the incidence of thyroid autoimmune bodies in the sera were the tanned erythrocyte agglutination (T.E.A.) test and the complement-fixing capacity (C.F.) by the method of Roitt and Doniach.

Positive results in the T.E.A. tests were obtained in 106 (77%) of the 138 hypothyroid cases, but no statistically significant difference could be demonstrated between any of the four well defined groups of hypothyroidism. In the euthyroid patients positive T.E.A. test results were as common after surgery as after 1311 therapy, but less common than in the hypothyroid groups. The number of positive C.F. tests varied considerably in the four hypothyroid groups, ranging between 47 and 87%. In particular, it was shown that in hypothyroidism induced by ¹³¹I the incidence of positive C.F. tests was significantly higher than in idiopathic and postoperative hypothyroidism, and that the C.F. tests showed higher titres in hypothyroidism due to chronic thyroiditis than in the other hypothyroid groups. In the thyroidectomized cases the C.F. test was positive equally often in hypothyroid and euthyroid cases. In none of the hypothyroid groups was any variation found between the number of positive T.E.A. tests and the duration of treatment with thyroid extract. The number of positive C.F. tests decreased with increasing duration of thyroid treatment in idiopathic hypothyroidism, but not in the other groups.

In discussing their findings, the authors point out that the frequency with which antibodies were demonstrated (namely, 87% by one or both tests) was similar to that reported by other workers, who had also noted a higher frequency of positive results in the T.E.A. test than in the C.F. test. This variation would support the thesis of Trotter et al. that the two tests reflect separate immune systems. They conclude that their findings indicate that the development of hypothyroidism is associated with some immunological process and the significantly higher incidence of a positive C.F. reaction in postparadiation hypothyroidism than in postoperative hypothyroidism suggests that the immunological mechanism is more active in the former group. They suggest that this finding may be tentatively explained by the hypo-

thesis that the radiation thyroiditis produced by ¹³¹I initiates an autoimmunological process resembling or identical with that in chronic thyroiditis. The demonstration of circulating antibodies in thyroid disorders other than chronic thyroiditis supports the view that several types of injury to the thyroid gland are capable of initiating a cycle of antibody formation, but the unspecific appearance of antibodies in a variety of thyroid disorders limits the value of serological tests.

In regard to the clinical significance of their findings the authors make two main points: (1) the presence of high antibody titres in a hypothyroid patient suggests thyroiditis as the likely cause of the disease; and (2) the presence of antibodies in thyrotoxic patients might be regarded as a contraindication to treatment with ¹³!I on account of its demonstrated tendency to cause hypothyroidism. They suggest, however, that the enthusiasm for the autoimmune hypothesis should not be allowed to obscure the possibility that all or some of the immunological abnormalities may be products of the disease and not necessarily actiological.

John Lister

907. The Use of Radioactive Phosphorus in the Diagnosis of Thyroid Cancer

N. B. Ackerman and J. F. Marvin. *Radiology [Radiology]* 77, 793-798, Nov., 1961. 4 figs., 13 refs.

A technique for the diagnosis of thyroid cancer using radioactive phosphorus (^{32}P) has been developed at the University of Minnesota Medical School, Minneapolis. The ^{32}P -uptake test has been performed on 61 patients with solitary nodular and multinodular goitres. The patients were given 500 μ c. of the radioactive material, and the uptake (selectively increased in malignant tissue) was tested 24 hours later. Counting was done with an eye-probe Geiger-Müller tube over the thyroid nodule and over the surrounding areas. Background counts averaged 10 counts per minute (c.p.m.) and counts over normal thyroid tissue about 110 c.p.m. An increase in ^{32}P uptake over the nodule of $20^{\circ}/_{\circ}$ or more was recorded as a positive result.

Seven of the 61 patients were considered to give a positive response, and 6 of these proved at operation to have a malignant tumour, the 7th having thyroiditis. In the 54 cases in which the test was negative the ³²P uptake over the nodules did not exceed the control value by more than 16% and the lesions were considered benign.

G. B. West

908. Hashimoto's Disease in Uniovular Twins W. J. IRVINE, A. G. MACGREGOR, A. E. STUART, and G. H. HALL. Lancet [Lancet] 2, 850-853, Oct. 14, 1961. 3 figs., 25 refs.

No definite genetic predisposition to Hashimoto's disease (lymphadenoid goitre) has as yet been proved. The disease was diagnosed from the results of clinical, biochemical, and serological investigations in both members of two pairs of uniovular twins. The findings lend support to the view that the disease is due to an abnormal antigen-antibody reaction and that the capacity to produce certain types of antibody is genetically determined. The authors state that the hypothesis of a

genetically determined disorder of immunological physiology explains the clinical observations better than any concept based on a purely chance phenomenon, such as a spontaneous somatic mutation.

G. B. West

ADRENAL GLANDS

909. Cortisone-DOC Therapy of Addison's Disease: Probable Insignificance of Dysadrenocorticism
T. S. DANOWSKI, F. M. MATEER, S.-N. MAFI, D. C. BORECKY, W. R. BALASH, and A. C. HEINEMAN JR. American Journal of the Medical Sciences [Amer. J. med.]

Borecky, W. R. Balash, and A. C. Heineman Jr. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 585-598, Nov., 1961. 7 figs., 34 refs.

Thirteen Addisonian patients treated up to 10 years by annual implantation of two pellets of deoxycorticosterone acetate and daily ingestion of about 25 mg. of cortisone and 20 mg. of hydrocortisone usually had essentially normal levels of serum CO₂, Cl, Na, K, Ca, inorganic phosphorus, albumin, globulin and cholesterol during periodic examination. Occasional low fasting blood sugar, serum sodium, and serum CO levels and slight elevations in blood NPN and serum potassium were recorded.

The excretion of water loads remained delayed in most of the patients with Addison's disease under treatment. A tendency to fasting hypoglycemia in these treated Addisonian patients did not affect the usual rises in blood sugar during oral or intravenous glucose tolérance tests. This was also true of the serum inorganic phosphorus decrease, indicating that the disposal of carbohydrate occurred at a comparable rate in the two groups. During-insulin tolerance tests the degree of hypoglycemia and hypophosphatemia was the same in treated hypoadrenocorticism and in controls, indicating that the tendency to fasting hypoglycemia represented a homeostatic adjustment and that carbohydrate metabolism was grossly normal. Urinary 17-ketosteroids tended to remain low and the 17-OH-corticosteroid (Porter-Silber chromogen) excretion was normal in patients on DOC and cortisone and hydrocortisone.

Despite residual hyperpigmentation and other evidences of incompletely corrected hypoadrenocorticism, the patients have felt well. There was, however, a definite trend to obesity because of the excellent appetite. There have been no deaths. An adrenal crisis occurred in one patient who omitted hydrocortisone during a period of gastroenteritis. The origins of such crises and remedial measures are discussed.—[Authors' summary.]

910. Adrenocortical Function and Cortisol Metabolism in Old Age

C. D. West, H. Brown, E. L. Simons, D. B. Carter, L. F. Kumagai, and E. Englert Jr. *Journal of Clinical Endocrinology and Metabolism* [J. clin. Endocr.] 21, 1197–1207, Oct., 1961. 3 figs., 23 refs.

To determine whether adrenocortical function declines with age the authors, working at the Veterans Administration Hospital, Salt Lake City, Utah, have compared a group of 15 men aged 25 to 40 with another group of 50 men aged 60 to 96, divided by decades, in respect of

cortisol metabolism and adrenocortical function and conducted parallel studies-of renal, hepatic, and thyroid function. Standard infusions of cortisol (1 mg. per kg. body weight) were administered intravenously and the concentration of free and conjugated 17-hydroxycorticosteroids in the plasma and urine determined. ACTH (corticotrophin) stimulation tests were performed with a dose of 25 units given intravenously.

No significant changes in adrenocortical function with advancing age could be shown by the criteria of 8-a.m. plasma levels of 17-hydroxycorticosteroids and the plasma corticosteroid response to ACTH stimulation. However, the urinary 17-hydroxycorticosteroid excretion decreased significantly and progressively with age and intravenously administered cortisol disappeared from the circulation at a significantly slower rate in old than in young men: after the dose the maximum plasma levels of conjugated 17-hydroxycorticosteroids were the same at all ages, but the decline from the peak was slower in the older men. At the same time the old men showed significant increases in blood urea and "bromsulphalein" retention and a significant decrease in endogenous creatinine clearance and basal metabolic rate. The plasma-bound iodiné level and uptake of radioactive iodine were unaffected by age. The authors suggest that these observations could be explained by decreased cortisol catabolism by the liver and other tissues and impaired renal excretion of its metabolites. The thyroid gland does not seem to be involved. J. N. Agate

911. Aldosterone and Oedema. (Aldostérone et oedèmes)

R. S. MACH and A. F. MULLER. Presse médicale [Presse méd.] 69, 2117-2120, Nov. 11, 1961. 7 figs., 32 refe

This paper from the University of Geneva reports observations on the role of aldosterone in normal subjects and in patients suffering from cardiac dysfunction. The relation between aldosterone secretion and the occurrence of oedema is not as simple as was first thought. It is known that as the body loses water and salt there is increased secretion of aldosterone, which causes retention of salt, thereby maintaining the dynamic equilibrium of the blood—hence this hormone has been named "the salt-saving corticoid". There have, however, been reports of raised urinary aldosterone excretion in oedematous patients and also of cases of hyperaldosteronism without oedema but with a lowered serum potassium level and polyuria, indicating that aldosterone can cause pathological retention of sodium.

The authors have therefore studied the effect of more prolonged administration of aldosterone in a normal subject and in patients with oedema. A healthy woman was given by injection 3 mg, of aldosterone per 24 hours. For the first few days there was a gain in weight of 2 to 3 kg, due to marked retention of water and sodium, but after 5 to 10 days of continued administration diuresis and increased excretion of sodium occurred and persisted for the duration of the experiment. It thus appeared that aldosterone continued to exert its action on the renal tubules, but that after a few days a com-

pensatory mechanism opposed this effect through an increase in blood flow which accelerated glomerular filtration and the recovery of sodium from the distal part of the tubules. The latter effect is known as the "escape phenomenon". Furthermore the same subject, after the occurrence of the "escape phenomenon", was given an increased dose of aldosterone (6 mg. per 24 hours) whereupon salt and water retention again occurred for 3 days followed by a second "escape". In addition, there was an over-all loss of potassium, as in Conn's syndrome.

In certain diseases, however, the compensatory mechanism observed in normal subjects does not operate, either because the body does not respond by an increased blood flow or because the greater blood flow does not increase glomerular filtration. This is observed in infantile nephrosis and in other conditions in which there is increased capillary permeability to albumin, so that water and salt pass into the interstitial spaces and cause oedema. Also patients with poor cardiac function suffer from diminished renal blood flow, so that glomerular filtration cannot be increased and hence the compensatory mechanism cannot be brought into play and no "escape phenomenon" occurs. This was shown in a patient with congestive cardiac insufficiency to whom aldosterone was administered. It seems that oedema occurs only if the compensatory mechanism fails to operate. The authors discuss the significance of these observations and conclude that aldosterone is not the primary cause of oedema but that it intervenes in a secondary capacity to increase retention of sodium and resistance to treatment with diuretics. Nancy Gough

PANCREAS

912. The Clinical Picture and Pathomorphology of Insulin Adenomata of the Pancreas. (К вопросу о клинике и потоморфологии островковых аденом поджелудочной железы)

A. M. HELIMSKIJ. Проблемы Эндокриноловии и Гормонотерапии [Probl. Endokr. Gormonoter.] 7, 78-82, Nov.-Dec., 1961. 2 figs., 27 refs.

Among the various types of insular adenoma of the pancreas it is necessary to distinguish: (1) those hormonally active; these consist of β cells and cause hypoglycaemia; (2) those composed of α cells, which cause hyperglycaemia through increased secretion of glucagon; and (3) those composed of hormonally inactive C and D cells, which produce other abdominal symptoms such as "acute abdomen" or intestinal obstruction, or may even cause no symptoms at all and are discovered only by chance at necropsy.

The author describes one case of the second type and one of the third. The first patient, a man aged 59 who had previously suffered from hypertension, suddenly developed vertigo, weakness, dry mouth, and severe glycosuria with acetonuria. His blood sugar level was found to be 592 mg. per 100 ml. He was treated with 72 units of insulin and given 130 g. of glucose daily, but pneumonia supervened and he died in a few days. At

necropsy two yellowish tumours measuring 1.5 x 1 and 1×1 cm. respectively were found in the pancreas between the head and the body, while smaller tumours of the same type were found in the tail. Histological examination revealed columns of cubical cells containing deeply stained pigment and argyrophil granules. The other patient, a man of 67, with tumour of Type 3, was admitted with signs of acute intestinal obstruction. Laparotomy revealed a yellowish mass the size of a goose. egg in the pancreatic region, which was unfortunately diagnosed as pancreatitis and he was given an intracapsular injection of penicillin. The same night he collapsed and died. At necropsy the mass was found to be a large multilobular tumour of the pancreas, composed partly of cylindrical cells which showed no argyrophil granulation and were similar to those of the walls of the secretory ducts and partly of polygonal cells with clear flask-like nuclei, resembling islet cells. In some areas there was degeneration of the cells and minute patches of calcification. L. Firman-Edwards

913. The Inner Ear in Diabetes Mellitus: Histological Studies

M. B. JORGENSEN. Archives of Otolaryngology [Arch. Otolaryng.] 74, 373-381, Oct., 1961. 3 figs., 32 refs.

That diabetes mellitus may be associated with changes in the inner ear, usually manifested by a slowly advancing bilateral deafness, but at times by Ménière-like attacks. has been known for at least 60 years, but only recently has thorough investigation been possible. Since the life of diabetics can now be prolonged by the use of insulin, late effects such as retinal, arterial, and neurological changes have been increasingly common. Lundback held that there is a vascular disease specific for diabetes which he termed "diabetic angiopathy". The retinal and renal changes are pure manifestations of this condition, while coronary arterial disease and vascular occlusion in the lower limb are regarded as "mixed types". This view is supported by the discovery of material staining positive with periodic-acid-Schiff (P.A.S.) stain in the retinal and renal lesions of diabetics. Further work, using P.A.S. staining, has shown such changes in the placenta of diabetic mothers, accompanied by endarteritis of the arterioles of the villi.

However, as the present author remarks, there is not yet enough evidence to prove that diabetics suffer from generalized vascular change, and in this post-mortem investigation carried out at Rigshospitalet, Copenhagen, he confined himself to the study of angiopathy in the diabetic inner ear, the temporal bones of 32 diabetics being examined. The middle ear was normal in all but 4 cases, in 2 of which there was a serous exudate, in one a purulent exudate, and in one an otosclerotic focus, but none of these influenced the inner ear findings. In the inner ear P.A.S. staining of the blood vessels of the stria vascularis showed that the changes were restricted to the capillaries of the stria; the capillary network of the spiral ligament was not affected, nor was the rest of the capillary net in the vestibular labyrinth. The strial changes were related to the duration of the disease and not to the patient's age. There was marked correlation between

strial change and renal lesions and between retinal and difficult to obtain a therapeutic reducing diet and to strial changes, but none between strial change and cerebral arteriosclerosis. The general conclusion drawn from this study is that there is a diabetic angiopathy, but that it is not generalized and shows a predilection for certain capillary systems—in the inner car only for the stria vascularis.

[This is a valuable paper, which should be studied in full for the statistical and histological data it contains.]

F. W. Watkyn-Thomas

914. Intelligence of Children with Diabetes Mellitus M. Ack, I. Miller, and W. B. Weil Jr. Pediatrics [Pediatrics] 28, 764-770, Nov., 1961. 2 figs., 15 refs.

I.Q. tests were administered to 38 pairs of diabetic and nondiabetic children. In each family the nondiabetic child was a randomly selected sibling of the diabetic child. No relation was found between I.O. difference (diabetic I.O.-sibling I.O.) and duration of illness. Children in whom diabetes began before the age of 5 years had significantly lower I.Q.'s than their nondiabetic siblings. There was no statistical difference between the diabetic and his sibling when the disease began after 5 years of age. A suggestive relationship (but not statistically significant) was found between the number of episodes of hypoglycemia and acidosis and the magnitude of the I.Q. difference between diabetics and siblings for those with onset of disease before 5 years of age.—[Authors' summary:]

915. Sex and Diabetes Mellitus: a Comparative Study of 26 Negro Males and 26 Negro Females Matched for

R. S. Anderson and L. M. Gunter. American Journal of the Medical Sciences [Amer. J. med, Sci.] 242, 481-486, Oct., 1961. 7 refs.

In this study from the Diabetic Clinic of the Department of Internal Medicine, Meharry Medical College, Nashville, Tennessee, 26 unselected male negro diabetics were compared with 26 unselected negro females matched for age. There was no notable difference in duration of diabetes in the two groups, the mean duration for males being 7.0 years and for females 8.0 years and only 11.5% of both having had diabetes for more than 16 years.

The women were significantly more obese than the men, only 16% of the women not being obese compared with 52% of the men. This is attributed to the fact that the men in this population were likely to be engaged in regular physical labour, whereas the women had low standards of housekeeping, requiring little expenditure of energy. No difference in the methods of treatment was established [but a larger series might have revealed that the proportion of women treated by diet alone was significantly greater than that of the men].

The men had a significantly better average level of control than the women, although 25% of the men were poorly controlled compared with none of the women, suggesting that more of the men had severe diabetes. This, the authors believe, also reflects "the socioeconomic and emotional status and the lowered activity level of these female patients: factors which make it

deny oneself of eating, one of the few pleasures available". Although no significant difference in the cardiac status of the two groups could be proved, angina, myocardial infarction, and cardiomegaly appeared to be more common in the women. These data confirm the higher incidence of coronary arterial disease in female diabetics compared with non-diabetics.

A. Gordon Beckett

916. Gastric Emptying in Diabetes Mellitus. English

G. DOTEVALL. Acta medica Scandinavica [Acta med. scand.] 170, 423-429, Oct., 1961. 22 refs.

Gastric emptying in diabetes has been shown to be delayed, especially in those with neuropathy. In this study carried out at Sahlgren's Hospital, Göteborg, Sweden, the author compared the gastric emptying times in 15 healthy medical students and doctors (average age 26 years) with those in 22 diabetic patients, of whom 14. (average 44 years) had no diabetic complications, no gastro-intestinal symptoms, and a mean duration of diabetes of 4 years, while the remaining 8 patients (average age 38 years) had marked diabetic retinopathy, nephropathy, and/or neuropathy, the mean duration of the disease being 17 years. The test meals, which were carried out after at least 12 hours' fasting, were of two different kinds, one consisting of 750 ml. of saline solution containing 100 mEq. NaCl per litre and the other of 750 ml. of a solution containing 30 mEq. of sulphuric acid plus 50 g. of sucrose in 1 litre of distilled water. Phenol red was added to allow calculation of the volume of gastric contents passing into the duodenum, and all the saliva was aspirated during the period of ingestion. Withdrawal of fluid from the stomach was begun 9 minutes. after introduction of the saline solution and 29 minutes after the acid and sucrose solution and completed in 2 minutes in both cases. The volume of gastric contents which had left the stomach during the period was calculated according to the method of Hunt and Spurrell [J. Physiol. (Lond.), 1951, 113, 157].

It was found that after the saline test meal gastric emptying was more rapid in the patients with uncomplicated diabetes than in the normal controls, but diabetics with late complications showed slower emptying than either of the other two groups. After the test meal of acid and sucrose there was no constant difference in the rate of emptying between the controls and patients with uncomplicated diabetics, while the number of patients with severe complications (3) was too small to allow of any safe conclusion. Gastric acid secretion in response to the saline test meal was about twice as high in the control cases as in diabetic patients.

In discussing the more rapid gastric emptying in diabetics without complications after the saline test meal the author points out that hydrochloric acid has an inhibiting effect on gastric emptying and suggests that the more rapid emptying in this group may have been due to reduced secretion of hydrochloric acid. He further considers the possibility that diabetics may have a lower duodenal sensitivity than healthy subjects to the minimal stimulating properties of saline, which would

explain the more rapid emptying in them than in the control group. In the patients with late diabetic complications it is possible that diabetic angiopathy in the stomach wall might cause diffuse damage to the gastric musculature and so result in slow gastric emptying in these patients. Neuropathy affecting the autonomic nervous system could bring about the same functional result as vagotomy and give rise to gastric atony with retarded emptying as a result. Diabetic diarrhoea is often combined with gastric retention. John Lister

917. Effects of Long-term Sulfonylurea Treatment on the Haematopoletic System of Diabetic Patients. [In English]

T. JAKOBSON. Annales medicinae internae Fenniae [Ann. Med. intern. Fenn.] 50, 83-93, 1961. 2 figs., 24 refs.

Peripheral blood and platelet counts were carried out on 66 diabetics on long-term treatment with carbutamide at the Maria Hospital, Helsinki. The mean neutrophil count was 2,720 per c.mm. and was significantly lower than in 19 patients taking tolbutamide (mean 3,640 per c.mm.) and in 32 healthy controls (mean 3,400 per c.mm.). A large number of the first group had counts between 2,000 and 1,000 per c.mm. and there was no difference between those receiving continuous and those having intermittent treatment. In 10 patients the sternal marrow was examined and showed definite toxic changes with thickening of nuclear chromatin and vacuolization of leucocytes. Eosinophilia was often present. In 37 of the 66 patients taking carbutamide there was thrombocytopenia, the average count being 155,000 per c.mm., and this was also found in about half of the patients given tolbutamide.

Drug hypersensitivity appears to be the responsible factor and caution is therefore necessary in the use of these oral diabetic drugs.

Arnold Pines

918. The Present Position of Oral Treatment of Diabetes: Experience with 3,000 Diabetics. (Der heutige Stand der peroralen Diabetestherapie nach Erfahrungen an 3000 Diabetikern)

A. LENHARDT. Whener klinische Wochenschrift [Wien. klin. Wschr.] 73, 698-702, Oct. 13, 1961. 5 figs.

On the basis of his experience with over 3,000 diabetic patients at Lainz Hospital, Vienna, the author discusses at length the oral treatment of diabetes mellitus. While agreeing with the generally held view that the juvenile type of diabetes needs insulin, while that with onset in maturity tends to respond to treatment with the sulphonylurea derivatives or to one of the diguanide preparations, he points out that there are exceptions in both groups and that patients must be selected individually according to their response to treatment. Whatever the method, the aim is to achieve a fasting blood sugar level below 150 mg. per 100 ml., a postprandial level not exceeding 200 mg. per 100 ml., and a daily urinary sugar excretion of less than 5 g.

The author's drug of first choice is tolbutamide. If control is not achieved with this compound alone one of the diguanides is added as a trial, the combined therapy having the advantage that the latter drug can

then usually be given in relatively low dosage. Regular haematological examinations are recommended to detect the fortunately rare granulocytopenia which may occur, especially with the diguanidine compounds. The paper includes graphs showing the different type of response obtained in various patients.

H. F. Reichenfeld

919. The Hypoglycaemic Action of Phenformin: Studies in Diabetics after Short-term Therapy

W. J. H. BUTTERFIELD, I. KELSEY FRY, and M. J. WHICHELOW. Lancet [Lancet] 2, 563-567, Sept. 9, 1961. 5 figs., 34 refs.

The mode of action of phenformin ("dibotin") has been investigated in the Department of Experimental Medicine, Guy's Hospital, London, the drug being given. in clinical doses to 16 patients with diabetes of various clinical types. Tests were devised to study in all the patients the response to the administration of glucose, insulin, and glucagon before and after 7 to 10 days' treatment with phenformin in doses of 50 to 100 mg. daily, increasing to 150 to 200 mg, daily. Patients whose mean fasting blood sugar level fell by more than 10% were classed as "responders", and these numbered 10. Side-effects included nausea and unexplained ketosis. without loss of weight. The main facts demonstrated by the trial were: improved tolerance to orally and intravenously administered glucose-insulin, rise in blood pyruvate level, and normal hyperglycaemic response to glucagon infusion after successful phenformin therapy. It is suggested that in therapeutic doses phenformin acts by enhancing the action of insulin.

A. I. Suchett-Kaye

920. Diabetes Mellitus and Primary Carcinoma of the Pancreas

C. G. CLARK and P. E. G. MITCHELL. British Medical Journal [Brit. med. J.] 2, 1259-1262, Nov. 11, 1961. 20 refs.

During the period 1955-9 65 patients were seen at the Aberdeen Royal Infirmary with primary neoplasm of the pancreas. Ten of these also had diabetes mellitus and summaries are given of these cases. In one case the tumour was a sarcoma, but in all the others it was a carcinoma. In all except the sarcoma symptoms of diabetes preceded those ascribable to the neoplasm by a few weeks. All the 10 patients were over 60 years of age. None had the obese type of diabetes, and in each the diabetes was classed as moderate to mild.

During the period under review 638 new cases of diabetes in patients over 40 years of age were seen. Of these, 586 were of the stable type—overweight, relatively resistant to insulin, and with little tendency to ketosis. The unstable type, of which there were 52 cases, are usually underweight, tend to develop ketosis, and are sensitive to insulin. Of these patients 21 were over the age of 60 and 10 had a neoplasm of the pancreas.

It is suggested that symptoms of diabetes of the unstable type occurring in a patient over 60 years should give rise to a suspicion of carcinoma of the pancreas until this possibility has been eliminated.

E. H. Johnson

The Rheumatic Diseases

921. Antibody Production in Rheumatic Diseases. The Effect of Brucella Antigen

L. E. Meiselas, S. B. Zingale, S. L. Lee, S. Richman, and M. Siegel. *Journal of Clinical Investigation [J. clin. Invest.*] 40, 1872–1881, Oct., 1961. 3 figs., 20 refs.

The possibility that a disordered immune response is related to the development of the rheumatic diseases, regarding which previous reports have been highly conflicting, was investigated at the Maimonides Hospital and and the State University of New York Downstate Medical Center, Brooklyn, by observing the production of antibodies in 19 patients with rheumatoid arthritis, 11 with systemic lupus erythematosus, 5 with acute rheumatic fever, and 6 with acute nephritis, following the subcutaneous inoculation of 0.5 ml. of Brucella vaccine; a group of 27 hospital patients with miscellaneous disorders served as a control. Blood samples were usually obtained before inoculation and at 1, 2, and 3 weeks afterwards. In addition to the estimations of antibrucella agglutinin titres, the samples were also examined for L.E. cells, rheumatoid factor, isohaemagglutinin titres, antinuclear antibody titres (using a fluorescent technique), and antithyroglobulin antibodies. Serum proteins were examined by paper electrophoresis and the sedimentation characteristics of the antibrucella agglutinins, rheumatoid factor, and antinuclear antibodies were determined by ultracentrifugal analysis.

Although there was some overlap between individual patients in the various groups, the patients with rheumatoid arthritis and systemic lupus erythematosus showed a significantly greater rise in antibrucella agglutinin concentrations than did the control subjects. Thus the geometric mean of antibrucella titres at 2 weeks was 80 for the 27 control subjects, 555 for 13 patients with rheumatoid arthritis, and 400 for 10 with systemic lupus erythematosus: Some patients with rheumatoid arthritis and systemic lupus erythematosus also showed changes in the titres of certain of the other antibodies studied. Of the 11 patients with systemic lupus erythematosus 4 gave a positive result in the direct Coombs test, 3 of 7 with rheumatoid arthritis showed a rise in the level of rheumatoid factor, while antithyroglobulin antibodies occurred in 3 of 11 patients with systemic lupus erythematosus and in 5 of 15 with rheumatoid arthritis. None of the control subjects showed this abnormal type of response.

The nature of the non-specific response of certain of the patients with rheumatoid disease and systemic lupus erythematosus is unknown. The authors suggest that it may be a basic defect in some so-called "autoimmume" diseases. They consider that the hyper-response to Brucella antigen in these patients may be related to the known predilection the organism has for damaging mesenchymal tissue, which is the, "target tissue" in rheumatoid disease. Ultracentrifugal analyses revealed

that the antibrucella agglutinin, like the rheumatoid factor, belongs to the 19S class of γ globulin. Further work is in progress to investigate the possibility that all the responding antibodies belong to the 19S class.

Hewett A. Ellis

922. Treatment of Gout with Zoxazolamine. (Traitement de la goutte par la zoxazolamine)
S. DE Sèze, A. RYCKEWAERT, and M. F. KAHN. Presse médicale [Presse méd.] 69, 2181-2182, Nov. 18, 1961.

This article from the Hôpital Lariboisière, Paris, describes the use of a new uricosuric agent, 2-amino-5-chlorobenzoxazole (zoxazolamine) in the treatment of 19 cases of chronic gout. The average daily dose was 375 mg. and there was a mean reduction in the blood uric acid level by about one-quarter. In over half the patients gouty tophi decreased in size and the number of acute

attacks was reduced.

18 refs.

As regards side-effects, in one case the drug caused severe anorexia and had to be discontinued. In other cases mild digestive disturbances did not call for cessation of treatment.

G. S. Crockett

923. Treatment of Systemic Lupus Erythematosus with Steroids

REPORT TO THE MEDICAL RESEARCH COUNCIL BY THE COLLAGEN DISEASES AND HYPERSENSITIVITY PANEL. British Medical Journal [Brit. med. J.] 2, 915–920, Oct. 7, 1961. 17 refs.

The results of treatment with steroid hormones of 107 patients suffering from systemic lupus erythematosus over a minimum period of 2 years are described and compared with those reported by other authors.

The majority of symptoms are rapidly though not permanently relieved, but the effect on the mortality rate is uncertain in the absence of a control group. There is no doubt, however, that in individual patients the drugs are temporarily life-saving. The incidence of side-effects was felt to be remarkably low, and it is suggested that larger doses of steroid than those administered to this group of patients may be given for a longer time in patients not responding to treatment. There appeared to be no therapeutic advantages in using any one form of steroid hormone, but electrolyte disturbances will be less of a problem if the delta analogues are used. The E.S.R. [erythrocyte sedimentation rate] has not been found to reflect accurately the clinical state of the patient, and it is regarded as unwise to insist on maintaining a normal sedimentation rate using larger doses than are needed to keep the patient symptom-free.

At the present time, in the absence of a superior therapeutic agent, it seems imperative that patients ill with systemic lupus erythematosus should be treated vigorously with steroid hormones.—[Panel's summary.]

CHRONIC RHEUMATISM

924. "Polymyalgia Rheumatica"
J. W. Todd. Lancet [Lancet] 2, 1111-1113, Nov. 18, 1961. 15 refs.

This paper from Farnham Hospital, Surrey, déscribes "the clinical features, laboratory findings, and prognosis. in 20 cases of the obscure, long-continued illness which has been called "polymyalgia rheumatica.", observed by the author between 1952 and 1959. The ages of the patients when first seen ranged from 61 to 78 years and ...16 of them (80%) were females. The symptoms, which were insidious in onset, included headache, depression, general malaise, and widespread pains, particularly in the neck, back, and limbs, unassociated with arthritis. Night sweats occurred in 5 patients, of whom 3 were febrile, and 4 additional patients were also febrile. In 9 patients the widespread non-articular pain was not present. The author discusses his reasons for including these patients, but there is no evidence that they were suffering from a common disorder.

The erythrocyte sedimentation rate (E.S.R., Westergren) was considerably elevated in all cases (75 to 138 mm. in one hour). Many of the patients had a normochromic anaemia. In 13 patients tested the sheep cell agglutination test gave a negative result. In 8 cases the patients were treated by bed rest in hospital, and the remainder at home. Salicylates were given for relief of pain and 2 patients received phenylbutazone "which seemed to give greater relief than salicylates". Only one patient was given prednisolone. With this regimen all the patients improved, although in a few the E.S.R. remained abnormally high and in only 2 cases has it been persistently normal. In no case was death attributable to the disorder, the nature of which is unknown.

Hewett A. Ellis

925. Polymyalgia Rheumatica: a Mismomer? E. N. Coomes and J. Sharp: Lancet [Lancet] 2, 1328-1331, Dec. 16, 1961. 7 figs., 10 refs.

In 5 subjects with symptoms similar to those described as "polymyalgia rheumatica" who were examined at the University of Manchester Rheumatism Research Centre the technique of Kellgren was employed in order to assess the type and distribution of pain after stimulation of a number of central joints and ligaments. The sites included the joints of the shoulder-girdle, the subacromial bursa, the manubrio-sternal joint, the interosseus sacro-iliac ligaments, and the atlanto-axial interspinous ligament. After an intradermal injection of procaine, saline solution was injected into-the various sites.

Unilateral occipital headache was experienced by two subjects given the injection into the atlanto-axial interspinous ligament. So far as the acromio-clavicular joint was concerned, pain occurred 15 seconds after withdrawal of the injecting needle. The area of maximum pain was at the top of the shoulder and from this point the pain spread up the side of the neck and downwards over the deltoid muscle. Injection of the subacromial bursa gave rise to pain in the lower part of the deltoid

muscle and at the base of the thumb. Injection into the sterno-clavicular joint was followed by pain over the joint, over the sternomastoid muscle, and also over a small area of the trapezius, while injection into the manubrio-sternal joint produced unilateral pain about two costal spaces lower than the joint.

In all cases the distribution of the pain was similar to that experienced in cases of so-called polymyalgia rheumatica. The investigators conclude, therefore, that the syndrome of polymyalgia rheumatica is probably attributable to arthritis, mainly of the spine and limb girdles. In this context significance is attached to the fact that muscle abnormalities have never been detected in patients with the syndrome. By analogy, muscle pain may occur in ankylosing spondylitis, a disease in which the main pathological processes affect the spine.

- A. Garland

926. The Problem of the Antibody Nature of the Rheumatold Factor. [Monograph, in English]
K. Aho. Annales medicinae experimentalis et biologiae Fenniae [Ann. Med. exp. Fenn.] 39, 1-60, Suppl. 7, 1961. Bibliography.

927. Clinical Evaluation of the Serological Tests in Rheumatoid Arthritis. I. Normal Series Collected by Random Sampling. [In English]
K. Aho, H. Julkunen, V. Laine, N. Ripatti, and O.

K. Aho, H. Julkunen, V. Laine, N. Ripatti, and O. Wager. Acta rheumatologica Scandinavica [Acta rheum. scand.] 7, 201–208, 1961. 1 fig.

The authors, working at the Aurora Hospital, Helsinki, and the Rheumatism Foundation Hospital, Heinola, Finland, have studied the relationship between clinical and serological findings in rheumatoid arthritis, the series consisting of patients with known rheumatoid arthritis and normal subjects who had been randomly selected during a study of the prevalence of the disease in Heinola, a town with a population of 10,000, in which every 10th inhabitant over 15 years of age was examined. Clinical, examination was supplemented by radiography of the hands and feet and a lateral view of the cervical spine, and blood was taken for serological study, the following serological tests being carried out: the latex slide test, the bentonite test using one serum dilution, the latex tube test, and the Waaler-Rose test in which a titre of 64 or more was regarded as positive.

Clinical examination of the 539 persons in the study revealed 19 with definite and 31 with probable rheumatoid arthritis according to the diagnostic criteria of the American Rheumatism Association. In 5 of the 19 cases (26%) of definite rheumatoid arthritis at least one serological test gave a positive result. For the group of probable rheumatoid arthritis the corresponding percentage was 23. The titre in the Waaler-Rose test was low (in the range 64 to 128), whereas the patients being treated in hospital for rheumatoid arthritis had a titre in the range of 250 to 500. In the remaining 489 persons the proportion of positive results in the serological tests were as follows: Waaler-Rose test 1.6%, latex tube test 4.1%, latex slide test 4.9% and bentonite test 1.4%; the titre in the Waaler-Rose test was low in this group.

Only one serological test was positive in the great majority of subjects in the normal group, whereas in cases of rheumatoid arthritis usually several tests were positive concurrently.

C. E. Quin

928. Clinical Evaluation of the Serological Tests in Rheumatoid Arthritis. II. Hospital Series of Patients with Definite Rheumatoid Arthritis. [In English]
O. WAGER, N. RIPATTI, V. LAINE, H. JULKUNEN, and K. AHO. Acta rheumatologica Scandinavica [Acta rheum. scand.] 7, 209-218, 1961. 2 figs., 8 refs.

This further investigation [see Abstract 927] was carried out on 408 patients treated at the Rheumatism Foundation Hospital, Heinola, Finland, between 1958 and 1960, the diagnosis of rheumatoid arthritis being based on the clinical and radiological findings. regards functional capacity, the majority of the 408 patients, 128 men and 280 women, were in Classes II and III. The Waaler-Rose and latex tube tests were performed on all patients and the bentonite test in 260 cases. A positive Waaler-Rose reaction was obtained in 67% of cases and a positive latex tube test in 85%. Most of the positive results of the Waaler-Rose test were in the titre range 250 to 500, there being relatively few low positive results. The results of these two tests agreed in 324 cases. Of the cases negative in the latex test only 5 had a positive Waaler-Rose reaction, but the latex test was positive in 79 cases in which the Waaler-Rose test was negative. The latter test was positive in 41% and the latex test in 63% of patients who had had rheumatoid arthritis for less than 6 months; in those in whom the disease had been present for 6 to 12 months the corresponding percentages for the Waaler-Rose and latex tests were roughly the same as in the series as a whole, this latter finding suggesting that the tests may be of some help in early diagnosis of rheumatoid arthritis: Of the 260 patients in whom the bentonite test was performed it was positive in 44%, whereas in these patients the Waaler-Rose test was positive in 65% and the latex test in 82%. . C. E. Quin

929. Antirheumatic Potency of Chemically Modified Adrenocortical Steroids

E. W. BOLAND. American Journal of Medicine [Amer. J. Med.] 31, 581-590, Oct., 1961. 1 fig., 31 refs.

The author reports on the antirheumatic potency of a number of adrenocortical steroids which have been modified by slight deviations in chemical structure and which have been tested clinically at St. Vincent's Hospital (Medical School of the University of Southern California), Los Angeles. The influence of a single chemical modification in the structure of hydrocortisone or cortisone, such as fluorination at C-9, greatly increases the anti-inflammatory properties of the steroid, but also produces such marked sodium-retaining and potassiumlosing effects that it cannot be used systematically as an antirheumatic drug. On the other hand the introduction of a double bond at C-1-C-2 produces prednisone and prednisolone and increases the antirheumatic potencies about fourfold over the parent substances without a corresponding increase in electrolyte activity.

In the present study 32 corticosteroids containing 2 or more chemical modifications have been tested for antirheumatic activity. The method consisted in treating patients with active rheumatoid arthritis with an established steroid and then with the test substance in order to determine the dosage of each substance required to maintain equivalent clinical improvement. It was found, for instance, that 16α -methyl 9α -fluoroprednisolone (dexamethasone) was approximately 7 times as potent as prednisolone. It is stated that the requirements for antirheumatic potency are: a double bond between C-4 and C-5 in ring A; an oxygen atom at C-3, at C-11, and at C-20; and a β -hydroxy group at C-17.

Oswald Savage

930. The Treatment of Rheumatoid Arthritis with Chloroquine. (Über die Therapie der chronischen Polyarthritis mit Chloroquin)

T. BEHREND, F. HARTMANN, and B. Schlegel. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 86, 2037-2042, Oct. 27, 1961. 3 figs., 16 refs.

The authors of this paper from the University Polyclinic, Marburg, and the Municipal Hospital, Wiesbaden, stress the difficulty of assessing the efficacy of therapy in a disease such as rheumatoid arthritis in which a remission rate of 48 to 71% may be obtained in the first year of illness and in which, in the years to follow, 25% of cases improve spontaneously and an equal number deteriorate in spite of every known form of treatment. The good results claimed for chloroquine must be seen in the light of these facts. Consequently, in carrying out a clinical trial of chloroquine, the authors chose cases which had been under their care for months or years and required corticosteroids, phenylbutazone, and salicylates. Chloroquine was given in a dosage of 250 mg. daily for 3 to 4 months before a decision was reached as to its effect, that is, whether the dose of steroid could be reduced or omitted, or, alternatively, whether relapses had been prevented. Initially 44 patients with chronic rheumatism were thus treated and 16 were eliminated because of side-effects or for other reasons; finally, only 28 patients (20 with rheumatoid arthritis) took part in the long-term trial, taking chloroquine for an average of 17 months. Of these, 5 seemed to have been improved (though the result was not decisive in 4 cases), 11 remained unaffected, and 12 became worse. It was noted that the Rose-Wasler reaction, positive in 20 cases, was directly affected by chloroquine in 10 cases, the titre falling with administration of the drug and rising when it was left off, but the change bore no relation to the clinical state and was noted only with Svartz and Schlossmann's modification of the above reaction; the result of the latex fixation test was unaffected.

There appears to be no doubt that chloroquine has a special affinity for highly polymerized substances, including elements of connective tissue. Were it possible to exploit this phenomenon clinically, it might lead to a new concept in therapeutics either by variation of the nucleus itself, or by making use of the latter as a carrier of an "anti-rheumatic" substance. In the meantime, the value of the use of chloroquine in chronic rheumatoid arthritis is open to question.

D. Preiskel

Neurology and Neurosurgery

931. The Value of Chlorproethazine in Neurology. (La chlorproéthazine: son intérêt en neurologie)
J. Sigwald, D. Bouttier, and C. Raymondeaud.

Presse médicale [Presse méd.] 69, 2187-2189, Nov. 18, 1961. 6 refs.

The authors report their experience with a new phenothiazine derivative not unlike chlorpromazine in its structural formula, having a diethylamino group attached to the end of its side chain instead of a dimethylamino group as in chlorpromazine. Its main action seems to be in reducing spasticity and contractures in pyramidal and extrapyramidal lesions. The drug is given in increasing doses, and while 25 mg. may be sufficient to obtain the desired effect, in other cases it may be necessary to give as much as 250 mg. a day. Side-effects on high dosage include malaise, lassitude, sleepiness, and mild orthostatic hypotension. A few patients complained of these side-effects even on minimal dosage.

[If chlorproethazine proves to act as the authors suggest it will be a valuable therapeutic substance in the treatment of long-term neurological disorders.]

G. S. Crockett

DIAGNOSTIC METHODS

932. General and Local Bioelectric Reactions in the Presence of Brain Tumours; the Results of Electrocorticography with the Application of Functional Stimuli. (Общие и местные биоэлектрические реакции при опухолях головного мозга по данным электрокортикографии с применением функциональных нагрузок) В. S. Очилтамоч. Журнал Невропатоловии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1599–1607, No. 11, 1961. 5 figs., 5 refs.

This paper from the Institute of Neurosurgery, Leningrad, describes a study of cortical activity which was carried out during operations for removal of a brain fumour in 96 patients ranging in age from 17 to 60 years. The functional stimuli were auditory, visual, and proprioceptive and were of two kinds, one adequate so as to allow the character of the stimulus to be picked out from the exposed region of cortex, and one inadequate, as exemplified, say, by the recording of the response to light from the fronto-parietal cortex.

The general non-specific reactions of the cortex were investigated first. Cortex lying over tumour showed no change of activity on application of a stimulus. The surrounding cortex showed an increase of basic activity and an increased amplitude of the slow potentials or in some cases fast rhythms appeared. In areas remote from the tumour the stimulus resulted variously in complete or partial restoration of cortical activity or blockade of the rhythm. The optimal condition for registration of the non-specific response was more or less full preservation of the activity of the investigated portion of brain,

while the absence of response was thought to be due to disturbance of a functional unit comprising cortex and the reticular formation.

Next, the local specific reactions were studied by recording the primary response of the afferent areas of the cortex to various stimuli. A biphasic primary response to auditory stimuli was recorded from the superior temporal gyrus in a patient with basophil adenoma of the pituitary gland in whom the tumour was exerting pressure on the temporal cortex. The dependence of the second phase of the primary response on the spontaneous electrical activity of the brain seemed to be demonstrated by its reduction in amplitude at the moment of full suppression of cortical electrical activity during operative interference for the removal of the tumour. In none of 22 cases of intracerebral tumour affecting the temporal lobe in greater or lesser dègree was any primary response registered on auditory stimulation. A case of arachnoid endothelioma of the left lateral ventricle gave a specific cortical response which was inhibited (presumably through activation of the reticular formation) by increasing the frequency of sound stimuli. In none of the cases operated on under local anaesthesia only was there any local response to sound stimuli, and where this response was elicited various neuroleptic drugs had been employed; presumably these drugs were blocking the ascending reticular formation. A failure to evoke any response to light stimuli was thought to be due to the inaccessibility of Brodmann Area 17. Passive finger movements evoked a response in the region of the central sulcus, although not when there was a motor disturbance on the side opposite to the tumour when the tumour lay near the motor-zone, or when background activity was preserved.

The author concludes that these results show that the optimal conditions for registering the primary cortical response are functional preservation of the sensory area as well as distinct lowering of its background activity, and the findings confirm in main outline previous experimental work concerning the presence of complex mechanisms of interaction between specific and non-specific thalamo-cortical structures. G. P. McGovern

933. Electroencephalographic Changes in Cerebellar Degenerative Lesions

L. A. LIVERSEDGE and V. EMERY. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 326-330, Nov., 1961. 18 refs.

It has been well recognized that cerebellar tumours are associated with abnormalities in the electroencephalogram (EEG). The mechanism by which this is caused is uncertain and some workers have suggested that the obstructive hydrocephalus may be the cause.

This paper from the University and Royal Infirmary, Manchester, reports the cases of 21 patients with various

types of cerebellar degeneration-in 2 this was predominantly spinal, in 4 spino-cerebellar, and in 15 predominantly cerebellar. In the spinal cases the EEG was within normal limits although there was some random theta activity. In 3 of the 4 spino-cerebellar cases the only-abnormality was a tendency to theta outbursts: in the 4th patient, who had epilepsy and optic atrophy as well, the recording showed high-voltage delta activity posteriorly on both sides. The 15 cerebellar cases, however; showed abnormalities which were essentially (1) a tendency towards slowing and forward spread of the dominant rhythm in 12, (2) excess of theta activity in all 15, and (3) delta activity in 12, in 4 of whom it was focal. In 3 cases the basal ganglia were thought to be involved, but in these the EEG was no different from the others. These findings suggest that EEG abnormalities are quite independent of increased pressure and that cerebello-central connexions may be the important

(Full details, clinical and pathological, are given of 3 fatal cases in the series, with brief summaries of the others.)

N. S. Alcock

CONGENITAL DISEASES

934. Studies in Spina Bifida Cystica. I. General Survey and Reassessment of the Problem

P. A. DORAN and A. N. GUTHKELCH. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 331-345, Nov., 1961. 45 refs.

This communication studies a series of 307 consecutive personal cases of spina bifida seen during a 10-year period [at the Royal Manchester Children's Hospital]. Of these, 96.7% have been traced and the minimum period of follow-up of the survivors is $2\frac{1}{4}$ years.

Spina bifida cystica is a more serious condition in females than in males. Only, 50% of all female infants with myelomeningocoele were judged fit for operation on the basis of degree of neurological deficit and of hydrocephalus as against 63% of males. Of all female cases of myelomeningocoele, whether operated upon or not, 40% survived as against 46% of males.

The timing of the surgical repair of the spinal defect is discussed and the operative technique described. Routine operation in the first few days of life seems to present no significant advantage. Repair of the spinal defect does, however, greatly reduce the risk of death from meningitis and brings no real additional risk of hydrocephalus. It rarely causes any deterioration in neurological status. One hundred and ninety-seven, or 64%, of the patients in this series were deemed fit for operation on the spinal defect, and of these, 156 (79%) survived.

The occurrence of hydrocephalus in cases of spina bifida cystica is almost invariably associated with an extensive malformation of the hind brain hitherto known as the Arnold-Chiari malformation. In the light of recent work on the pathogenesis of this condition, it is suggested that it be known as "encephalo-cranial disproportion". Despite the abnormalities in structure of the brain in encephalo-cranial disproportion there is no

evidence that the condition is in itself incompatible with normal intellectual status. On the contrary, if the hydrocephalus is arrested either spontaneously or by surgical means, the ultimate intellectual status of the majority of survivors is normal. Of the 156 known survivors in this series, 33% show no significant neurological disability and more than half of the remainder are mainly handicapped by incontinence. Almost every child who has any power in the proximal muscle groups of the legs can eventually be enabled to walk with the appropriate orthopaedic assistance, either by way of operation or by the provision of suitable appliances.

There are 20 patients with total paraplegia still alive, and investigation into their present status suggests that further long-term survival is not unlikely. While episodes of urinary infection and especially of the appearance of bed-sores have occurred in the majority of cases, they have proved amenable to treatment in hospital, and of the paraplegic infants and children who have not survived, only 3 are known to have died of urinary infection, and none of the effects of bed-sores.

In the light of these findings, it can be argued that the most important remaining limit to the number of infants born with spina bifida cystica of all grades of severity who can live a worthwhile, even if restricted, life, is the amount of medical and surgical care which can be expended upon them.—[Authors' summary.]

BRAIN AND MENINGES

935. A New Sternal Reflex in Cases of Severe Cerebral Damage

N. BANIEWICZ. British Medical Journal [Brit. med. J.] 2, 1675–1678, Dec. 23, 1961. 1 fig., 34 refs.

The author, from the Neurological Department of the General Hospital, Bydgoszcz, Poland, describes 2 distinct types of sternal reflex which can be elicited in the unconscious or stuporous patient with cerebral damage. The more common type of sternal reflex consists of unilateral or bilateral movements of the upper limbs directed towards the removal of a painful stimulus when applied to the sternum. These movements are associated with autonomic reactions—namely, mydriasis, a rise in pulse rate and respiration rate, and increase in blood pressure. This sternal reflex occurs in conditions affecting the cerebral hemispheres and is of particular value in comatose patients when neurological examination has failed to determine the site of the lesion. In such cases the hemiplegic or hemiparetic side shows either no responses or defective responses, depending on the extent of the lesion.

Decerebrate reactions consisting of transient rigidity of the neck and limbs, which persisted for as long as a painful stimulus to the sternum was applied, was the second type of sternal reflex observed. This response occurred only with brain-stem lesions and was never seen when the cerebral hemispheres alone were affected. Clinical and necropsy findings in 7 illustrative cases in which one or other type of sternal reflex was elicited are presented.

A. G. Freeman

936. Cerebral Haemodynamics in the Sequelae of Cerebral Trauma in Older Patients. (Die cerebrale Hämodynamik bei Hirntraumafolgezuständen im höheren Lebensalter)

H. LENNARTZ. Deutsche Zeitschrift für Nervenheilkunde [Disch. Z. Nervenheilk.] 183, 54–62, 1961. 15 refs.

The observed discrepancy between the severity of a head injury and the extent of post-traumatic disability in older patients prompted the author to investigate the cerebral circulation in 12 patients; aged between 51 and 70 years, who had sustained a head injury 2 to 5 years before admission to the University Hospital, Hamburg-Eppendorf. All the patients complained of vertigo, headaches, and general physical and mental debility.

The results of the investigation of the cerebral circulation were compared with those in 13 control patients of similar age suffering from mental illnesses. No significant vascular abnormalities were found in the control group, and in 4 patients with the post-traumatic syndrome the findings were also normal. In 5 of the patients, however, the vascular resistance and mean arterial pressure were raised, and 3 showed diminished oxygen uptake. The post-traumatic group, as a whole, showed normal blood flow values, but the cerebral oxygen uptake was usually diminished and the vascular resistance and mean arterial pressure were increased. It is suggested that the haemodynamic abnormalities are the result of cerebrovascular disease or of undue ageing of cerebral tissue, and that the head injury only precipitated symptoms in a previous diseased brain. In the author's opinion the view that these symptoms are solely the result of psychological factors, such for example as impaired adaptability, in persons in the older age groups is untenable.

H. S. Schutta

937. Hypertrichosis after Cranio-cerebral Trauma to the Fronto-parietal Region. (Гипертрихов у больных после черепно-мозговой травмы теменно-лобной области)

E. P. PLATONOVA. Журнал Невропатоловии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1355—1358; No. 9, 1961. 2 figs., 3 refs.

The author reports from Altai Medical Institute the development of hypertrichosis in 14 out of 20 patients. with residual changes associated with extensive bony defects of the skull and scarring of the brain and meninges of the fronto-parietal region due to penetrating wounds sustained in the Second World War. The main neurological symptoms were periodic epileptic fits, attacks of paraesthesiae or spastic hemiparesis, and hemihypoaesthesia or hemianaesthesia on the side opposite to the lesion. In the 14 patients with-hypertrichosis the hair was distributed mainly in the scapular region on the side opposite to the cranial lesion, but in some cases also appeared on the upper anterior chest and over the shoulder joint, being accompanied in one case by pigmentation of the adjacent skin. These changes had not developed until some 10 years after the head wound had been received.

The groups with and without hypertrichosis were found to be similar in regard to the presence of atrophy of the muscles of the shoulder girdle and arm, of Horner's syndrome on the side of the motor and sensory disturbance in most cases, hyperhidrosis, and the frequent complaint of pain in the heart without discernible pathological cause. However, the patients with hypertrichosis generally developed epileptic fits of a focal character in contrast to patients without hypertrichosis, whose fits weregeneralized. Recording of the amplitude of the pulse from the skull defect or from the temporal artery while the patient performed a mental task showed in those with hypertrichosis either no change or a normal increase in amplitude on the side of the lesion and a paradoxical decrease in amplitude on the opposite side, whereas the patients without hypertrichosis most frequently showed this paradoxical reaction on both sides. In the hypertrichotic cases there were differences of skin temperature of more than 1° C. between the suprascular region, the lateral surface of arm and forearm, and the ulnar side of. the palm and back of the hand, whereas only the ulnar border of the hand showed any deviation in temperature in the non-hypertrichotic cases. About half the patients with hypertrichosis showed either periodic hyperaemia and swelling of the skin of the brow and orbital region. or cyanosis and cooling in the distal part of the hand on the side of the lesion, but such pronounced vasomotor disturbances were seen in none of the cases without hypertrichosis.

The author considers the hypertrichosis to be part of a dystrophic syndrome manifested at the level of the upper thoracic and lower and middle cervical segments of the cord and probably connected with lesions of the motor and sensory tracts.

G. P. McGovern

938. Reversal of Blood Flow through the Vertebral Artery and Its Effect on Cerebral Circulation
M. Reivich, H. E. Holling, B. Roberts, and J. F. Toole.
New England Journal of Medicine [New Engl. J. Med.] 265, 878–885, Nov. 2, 1961. 5 figs., 20 refs.

A reversal of blood flow in the vertebral arteries was demonstrated in 2 patients with symptoms of cerebral ischaemia who are described in this paper from the University of Pennsylvania School of Medicine, Philadelphia. The first patient was a man aged 40 who gave a history of left parietal headaches brought on by exercise and of attacks of transient paralysis of the left arm. Examination revealed reduction of the left brachial and radial pulses, a systolic bruit over the left subclavian artery, and reduced blood pressure and blood flow in the left arm. Compression of either carotid artery led to ipsilateral slowing of the encephalogram, paraesthesiae in the contralateral limbs, and on one occasion loss of consciousness. Arteriography revealed stenosis of the left subclavian artery just proximal to the origin of the left vertebral artery, and dye tests showed the dye flowing up the right vertebral artery into the basilar artery, then back downwards in the left vertebral artery. Retrograde flow in the left vertebral artery was confirmed by measurements of blood flow at operation on this patient, using a square-wave electromagnetic flow-meter. The second patient, a man of 58, presented with a short history of. attacks of visual blurring, aphasia, and paresis of the

right hand. His arteriogram showed complete occlusion of the left internal carotid artery, stenosis of the left subclavian artery proximal to the origin of the left vertebral artery, and retrograde filling of the left vertebral artery from the right vertebral and basilar arteries.

In animal studies retrograde blood flow in the left vertebral artery of 4 dogs was demonstrated by experimental occlusion of the left subclavian artery proximal to the origin of the vertebral artery. The reverse flow was almost equal to the forward flow before occlusion of the subclavian, and was accompanied by a compensatory increase of 78% in flow through the right vertebral artery. The other changes recorded in the dogs were an increase of flow through both common carotid and internal carotid arteries, and a reduction of 40% in total cerebral blood flow.

In a discussion of the findings the authors point out that the reduced total cerebral blood flow consequent upon the diversion of blood to the vertebral-basilar system may be responsible for symptoms of cerebral insufficiency in cases of this nature. Provided the posterior communicating arteries are adequate the base of the brain can be supplied largely from the carotid system. Obstruction of vessels within the thorax, as well as in the neck, can compromise the cerebral circulation, and the aim of arteriography must be to visualize the entire length of the vessels from the aortic arch to the intracranial branches.

Bernard Isaacs

939. The Prognosis of Survival from Cerebrovascular Accidents

I. D. MELVILLE and S. RENFREW. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 346-349, Nov., 1961. 6 refs.

In an attempt "to discover early clinical and electroencephalographic evidence which would allow confident prediction of life and death in cerebrovascular accidents " the authors, at the Royal Infirmary, Glasgow, have studied 85 patients with a stroke, in all cases within 7 days of onset. Patients with brain-stem lesions and those who had had convulsions were not included. 'In 79 of the patients an electroencephalogram (ECG) was recorded. Of 43 who died, the diagnosis was confirmed by necropsy in 31. An arbitrary grading of consciousness from 1 to 4 was used. There was a mortality of almost 100% in those who remained deeply unconscious for 12 hours or more. The EEG was grossly abnormal in 64 and normal in the remaining 15 cases, and the finding of a bilateral gross abnormality was associated with a mortality of 90%; with a normal EEG there was no mortality. In patients in an intermediate state of consciousness the EEG is considered to be of some value in assessing prognosis. · Hugh Garland

940. The Cluster Headache

R. C. DUVOISIN, G. W. PARKER, and W. L. KENOYER. Archives of Internal Medicine [Arch. intern. Med.] 108, 711-716, Nov., 1961. 21 refs.

A review is presented of the clinical features in 32 cases of a "particular variety of headache", which has been described in the literature under a number of terms,

including Sluder's headache, sphenopalatine neuralgia. periodic migrainous neuralgia, Harris's neuralgia, ciliary neuralgia, erythromelalgia of the head, histamine cephalgia, Horton's headache, autonomic facial cephalgia, greater superficial petrosal neuralgia, and "red migraine". The symptoms are unilateral, abrupt in onset, brief in duration, and appear consistently on the same side. A severe periorbital pain, often accompanied by lacrimation, conjunctival injection, and nasal congestion. is characteristic. Attacks are frequent, usually daily. for a period of 1 or 2 months and then subside to return only after an interval of months or years, following a pattern which has suggested the term "cluster headache". As in migraine, the pain of the cluster headache appears to be related to the dilatation of extracerebral cranial arteries. Manual occlusion of the ipsilateral common carotid artery in the neck often reduces the pain. Vasoconstrictor drugs, including adrenaline and ergotamine, relieve the headache, whereas vasodilator agents, including ethyl alcohol, nitroglycerine, amyl nitrite, and histamine, may aggravate or precipitate it. These features seem to link the cluster headache with migraine.

Most of the patients in the present series responded to 1 or 2 mg. of ergotamine by mouth daily, although a few needed 4 or 5 mg. daily for several weeks. No signs of ergot toxicity developed, but as a precaution some of the patients were advised to omit the ergotamine on one day each week.

J. MacD. Holmes

941. Impairment of Consciousness in Migraine E. R. BICKERSTAFF. Lancet [Lancet] 2, 1057-1059, Nov. 11, 1961. 8 refs.

The author has previously drawn attention (Lancet, 1961, 1, 15; Abstr. Wld Med., 1961, 30, 58) to attacks of migraine in which the early vascular disturbance appears to affect the distribution of the basilar artery. In the present paper he describes 8 patients, all adolescent girls, in whom the diagnosis of basilar artery migraine seemed justified and in whom there was loss of consciousness. The degree of unconsciousness was not profound and the patients were never unrousable. It is suggested that transient ischaemia of the reticular formation in the brain-stem is the cause of the alteration in consciousness.

The importance of the differential diagnosis from epilepsy and from syncope is emphasized.

J. W. Aldren Turner

942. Ocular Sympathetic Palsy in Periodic Migrainous Neuralgia

E. A. NIEMAN and L. J. HURWITZ. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 369-373, Nov., 1961. 14 refs.

A study of the clinical features of migrainous neuralgia as seen at the National Hospital, Queen Square, London, in 35 male and 15 female patients showed that the peak age of onset lay between 26 and 35 years (total age range 13 to 69), that the pain commonly increased in intensity for 15 to 30 minutes, lasted usually up to 2 hours (but in one case lasted all day), was usually con-

stant in each patient, and that its maximum severity was frequently (36 cases) in or above the eye; radiation of the pain occurred in 39 of the 50 cases. Associated features included lacrimation, suffusion of the eye, rhinorrhoea, nasal congestion, periorbital oedema, facial flushing, and dilatation and tenderness of the ipsilateral temporal. artery. The site and radiation of the pain suggested that dilatation takes place in the territory of the internal and external carotid arteries. A warm atmosphere, alcohol, worry, overwork, and stress were the commonest provoking agents. Among the methods of producing relief were pressure on the neck (4 patients), application of heat (2), of cold (2), and trilene inhalation (1). Frophylactic administration of 1 mg. of "cafergot" (containing ergotamine) as a suppository was effective, but it did not terminate a bout of attacks, so that this treatment must be continued until a natural remission is obtained.

Oculosympathetic paralysis was seen in 11 (22%) of the patients, in 10 cases being permanent. The authors state that this high percentage may have been due to the fact that cases without signs and responding well to treatment were not included in the hospital diagnostic index. The eye palsy may disappear or lessen between attacks and usually occurs in patients over 45 years of age. The most likely explanation is oedema or ischaemia of the internal carotid artery as a result of a thrombotic occlusion. If the 5th cranial nerve is involved, it is probable that, instead of periodic migrainous neuralgia being a relatively benign condition, there may be some structural lesion in the middle cranial fossa.

G. de M. Rudolf

943. The Drug Therapy of Migraine J. M. Sutherland and M. J. Eadle. Medical Journal of Australia [Med. J. Aust.] 2, 740-742, Nov. 4, 1961. 22 refs.

Different preparations of ergotamine tartrate were given at Brisbane Hospital, Australia, to 67 patients with migraine and 10 with periodic migrainous neuralgia. In 25 of the 67 with migraine, in whom electroencephalography revealed bilateral synchronous slow activity, the number of headaches was reduced by administration of phenytoin. In this dysrhythmic group 7 patients had a history of major seizures, 3 had psychomotor attacks, and 3 a family history of epilepsy. The 67 patients with migraine or dysrhythmic migraine were given at random one of the following treatment regimens: (1) a tablet containing 1 mg. of ergotamine tartrate and 100 mg. of caffeine taken half-hourly to a maximum of 6 tablets; (2) a similar tablet with a flavouring agent chewed without swallowing at half-hourly intervals until the headache was relieved, to a maximum of 6 tablets; (3) a tablet containing 0.6 mg. of ergotamine tartrate, 40 mg. of phenobarbitone, and 0.2 mg. of belladonna alkaloids, swallowed at intervals of one hour to a maximum of 3 tablets; and (4) 0.36 mg. of microsized ergotamine tartrate from an atomizer at 5-minute intervals to a maximum of 6 inhalations. It was found that the ergotamine was more effective if rapidly absorbed-that is, when given sublingually or by inhalation—than when it was swallowed.

944. Comparative Clinical and Morbid Anatomical Findings in the Assessment of the Results of Treatment of Cerebral Abscess. (Vergleich klinischer und pathomorphologischer Befunde zur Beurteilung der Behandlungsergebnisse beim Hirnabscess)

J. C. NAVARRO, F. GULLOTTA, and R. WÜLLENWEBER. Deutsche Zeitschrift für Nervenheilkunde [Dtsch. Z. Nervenheilk.] 183, 7-27, 1961. 6 figs., 40 refs.

The authors present an analysis of 92 cases of cerebral abscess seen at the University Neurosurgical Clinic, Bonn. The incidence was fairly uniformly distributed throughout the 5 decades 0 to 50 years, only 11 cases occurring in patients aged over 50; the ratio of males (74) to females was 4:1, and the origin of infection (posttraumatic in 34 cases) was known in all but 3 cases. Over half the surviving patients were severely disabled. In the 45 cases coming to necropsy most of the abscesses were multilocular, and only 15 showed the classic abscess capsule composed of 4 distinct layers. In 22 cases no definite layers could be identified at all: in 14 of these the capsule was diffusely infiltrated with inflammatory cells, while in 8 the capsule surrounding the main abscess was studded with minute foci of suppuration which disorganized the capsule structure. In the remaining 8 cases there was no capsule. Multiple abscesses were present in 25 post-mortem specimens.

Discussing the results of treatment, the authors point out that these cases varied greatly in many respects and a statistical analysis of the various methods of treatment was therefore impossible, even with this comparatively large number of cases. But in view of the high incidence of multiloculated abscesses and the finding of suppuration in some abscess capsules, early radical excision of the abscess where possible is probably the treatment of choice.

H. S. Schutta

945. The Clinical Diagnosis of Sporadic Spontaneous Encephalitis. (Zur klinischen Diagnose sporadischer Spontanencephalitiden)
G. HUBER. Nervenarzt [Nervenarzt] 32, 491–497, Nov., 1961. 22 refs.

The author discusses the clinical diagnosis of sporadic spontaneous encephalitis with reference to 13 such cases of undetermined aetiology observed at the University Neurological Clinic, Heidelberg. The presenting signs and symptoms included headache, various forms of mental disturbance, dysarthria, and a variety of abnormal movements; mild papilloedema was present in 4 cases. Of the 9 patients who died 3, aged 9, 12, and 17 years respectively, were examples of subacute sclerosing leucoencephalitis as described by van Bogaert. Of the other 6, who were aged between 20 and 64 years and who died within 2 to 7 weeks of onset post-mortem examination was performed on 5, when histological examination showed a non-specific inflammatory reaction in the white matter of the cerebrum and the caudal parts of the brain stem. The remaining 4 patients, aged between 12 and 30 years, recovered after 31 to 7 months although with some intellectual deficit. The findings in the cerebrospinal fluid and the electroencephalograms and possible actiological factors are discussed. H. S. Schutta

946. Positional Nystagmus of the Central Type as Evidence of Subtentorial Metastases

T. CAWTHORNE and R. HINCHCLIFFE. Brain [Brain] 84, 415-426, Sept., 1961. 49 refs.

Attention is drawn to the central type of positional nystagmus as an early sign of subtentorial metastases. In this central type the nystagmus appears as soon as the critical head position is assumed and continues as long as the position is maintained; it also reappears when the position is resumed. The accompanying vertigo is rarely severe. The authors, describe 6 cases of subtentorial metastases in which this physical sign was observed.

J. W. Aldren Turner

947. Evaluation of UK-738 in the Treatment of Extrapyramidal Disorders: Preliminary Communication T. FRIGYESI. Neurology [Neurology (Minneap.)] 11, 1050-1054, Dec., 1961. 1 fig., 16 refs.

UK-738 (methylbenztropine hydrobromide) has an anticholinergic effect, but it also has antiserotonin properties. The author, at Pineland Hospital, Pownal, Maine, has evaluated its use in 84 patients suffering from extrapyramidal disorders and compared it with trihexyphenidyl and benztropine methanesulphonate. Motion pictures of the patients were used to assess the effects of, the drugs. Double-blind methods were not employed, but the author considers that some of the results were so impressive that they could not be due to errors in observation. UK-738 was less effective in Parkinsonism than the other two drugs, but in athetosis, cerebellar tremor, and myoclonus it exerted a clear therapeutic effect not shown by the other drugs, and no side-effects were observed. J. W. Aldren Turner

DEMYELINATING DISEASES

948. Progressive Multifocal Leukoencephalopathy E. P. RICHARDSON JR. New England Journal of Medicine [New Engl. J. Med.] 265, 815-823, Oct. 26, 1961. 17 refs.

In 1958 Astrom et al. (Brain, 81, 93; Abstr. Wld Med., 1958, 24, 447) described a then hitherto unrecognized complication of chronic lymphatic leukaemia and Hodgkin's disease. In the 3 cases reported at that time the condition affected the white matter of the brain and was named "progressive multifocal leuko-encephalopathy". The present author has now made a study of 10 such Boston, and has also reviewed a further 12 cases reported in the literature.

The clinical and post-mortem findings in the entire group of 22 cases are presented in a table. On the average, the neurological disorder ran a course from onset to death of 3 to 4 months. The youngest patient died at the age of 31, the oldest at 82, and the mean age at death was 57 years. Men were affected by the disease twice as often as women. The condition was most frequently associated with Hodgkin's disease (6 cases) and chronic lymphatic leukaemia (4 cases); it was also observed in 3 cases of lymphosarcoma, in 2 cases each of chronic myeloid leukaemia, sarcoidosis, and carcinoma-

tosis, and in one case each of miliary tuberculosis, coronary disease, and advanced age alone respectively. The predominant clinical features were those of a rapidly progressive focal or diffuse, but asymmetrical, disorder of the brain, unaccompanied by increased intracranial pressure or by any significant changes in the cerebrospinal fluid. Spastic or flaccid hemiparesis occurred in 17 of the 22 cases and bilateral pyramidal signs were frequent in the terminal stage of the disease. Visual disturbances were noted in 12 cases and in 4 of these total blindness occurred. Pallor of the optic disks was observed in 2 cases, nystagmus in 2, and a lateral rectus palsy in one. Aphasia was present in 7 cases and dvsarthria in 6. Sensory hemianaesthesia was recorded in 4 patients, dysphagia in 4, cerebellar and brain-stem involvement in 2, unsteadiness of gait [not further specified] in 2, and generalized choreiform movements in one. Some degree of mental deterioration, personality change, or dementia occurred sooner or later in nearly every case. The electroencephalogram was abnormal in all 7 cases in which it was recorded, showing diffuse slow-wave (delta or theta) activity of a sort in no way distinctive of this disorder"

A review of the histological findings in the 22 cases shows that although the lesions were most numerous in the cerebral hemispheres, the brain stem and cerebellum were often also severely affected. No abnormality was found in the spinal cord. The author states that the combination of multiple demyelinating lesions of all possible gradations in size and stage of evolution with remarkable changes in oligodendrocytes, and often too in astrocytes, does not occur in any other disease known. to him. Evidence is cited which shows that the one factor common to all the chronic diseases met with in this series was the presence of "relative immunologic unresponsiveness", so that a decreased resistance to infections was only to be expected. The author suggests that this unusual demyelinating process resulting in this progressive disorder of the central nervous system running a relatively rapid course is consistent with an atypical form of virus infection. A. G. Freeman

949. The Problem of the Actiology of Disseminated Sclerosis. (Results of Electron Microscopy of the Cerebrospinal Fluid of Patients.) К вопросу об этиологии множественного склорова (данные электронной микроскопии спинномовговой жидкости больных) Е. D. Goryna. Журнал Невропатологии и Психифици [Ž. Nevropat. Psihiat.] 61, 1497–1503, No. 10, 1961. 4 figs., 7 refs.

This paper from the Kiev Clinic for Nervous Diseases and the Kiev Institute of Epidemiology and Microbiology presents the results of a search by electron microscopy for virus particles in the cerebrospinal fluid (C.S.F.) of 98 patients suffering from disseminated (multiple) sclerosis. The C.S.F. of 22 patients with other neurological disorders—neoplastic, traumatic, vascular, inflammatory, and allergic in type—and from a number of non-neurological surgical patients was also investigated. Preparation for electron microscopy was made as follows: a drop of C.S.F. was placed on a colloidal film, subjected

to suction and partial drying, and then dusted with chrome in order to increase contrast. The C.S.F. had previously been investigated to exclude pathological changes or the presence of bacteria.

In nearly all the cases of disseminated sclerosis identical round bodies 40 to 50 m μ in diameter were present. Their quantity depended on the stage of the illness: During an exacerbation the entire microscopical field - was covered with these bodies, but during remission or after treatment by intramuscular injections of a preparation of the patient's own C.S.F. they were reduced in number or had disappeared altogether. After treatment the bodies were often seen to be deformed. In none of the control cases except those with haemorrhagic and virus encephalomyelitis were these bodies seen. Since many of the control cases showed high C.S.F. levels of protein the author is disinclined to regard the bodies as simply particles of albumin. The cases of disseminated sclerosis were of all degrees of severity and the diagnosis was made according to the usual criteria. A number of case histories are given illustrating the effects of treatment both in reducing the number of bodies in the C.S.F. and achieving various degrees of remission.

At one point in the article the words "body" and "virus particle" are used interchangeably, but the author concludes by saying that although there appears to be a direct correlation between the presence of the bodies and the disease disseminated sclerosis, it is not yet possible to say that these bodies are viruses. G. P. McGovern

NEUROMUSCULAR DISEASES

950. Ocular Myasthenia. (Über die okulare Myasthenie)

W. Papst and E. Esslen. Klinische Monatsblätter für Augenheilkunde [Klin. Mbl. Augenheilk.] 139, 345-357, Oct., 1961. 8 figs., bibliography.

Ocular myasthenia, which is observed in over 50% of cases of myasthenia gravis and very often represents initially the whole syndrome, can give rise to diagnostic difficulties. Especially monoparetic cases, such as those in which only the superior palpebral levator or some other external eye muscle is affected, may be difficult to diagnose, particularly as the neostigmine and "tensilon' (edrophonium) diagnostic tests are very often negative in these cases. The tensilon test is preferable to the neostigmine test, as with the former the improvement in muscle action appears much more quickly and lasts longer and the side-effects are less than with the latter. The best results in diagnosis come from a combination of. electromyography with the tensilon test. Electromyography of a myasthenic muscle shows, after an initial short-lived interference pattern, loss of more and more motor units and decreasing amplitude. To differentiate this from a peripheral paresis tensilon is applied, whereupon the reappearance of interference and increase of. amplitude in the electromyogram provides evidence of myasthenia. Neostigmine is generally used for treatment, but pyridostigmine (" mestinon ") is better, especially in ocular myasthenia, and produces fewer side-effects,

Certain cases are resistant to treatment, perhaps owing to superadded myopathy; in such cases overdosage, with cholinergic crises, can easily be produced if the possibility is not guarded against.

L. Wittels

951. A Syndrome of Continuous Muscle-fibre Activity H. ISAACS. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 319–325, Nov., 1961. 5 figs., 13 refs.

This paper describes investigations carried out at the General Hospital, Johannesburg, in 2 cases of a syndrome hitherto unknown and bearing a superficial resemblance to myotonia. The first patient was a boy aged 12 who from the age of 5 had gradually developed increasing stiffness of the muscles, which had become severely incapacitating and was present day and night. The stiffness was increased by voluntary contraction. He was extensively investigated with largely negative results. Electromyography showed a state of constant rapid dysrhythmic discharge of independent muscle fibres; this persisted after local nerve block, but disappeared after infiltrating the muscles with procaine. Muscle biopsy showed non-specific changes and a variety of empirical forms of therapy proved useless.. The second patient was a man of 53 who complained of increasing stiffness of muscles over the previous 6 months. Electromyographic changes were similar to those in the first patient, as were also the changes in muscle biopsy specimens. Empirical treatment was again valueless and the patient continued to deteriorate until he was unable to walk. The effect of sodium hydantoinate (100 mg. 4hourly) was then tried and this was followed by immediate improvement so that in 6 months he was mobile and able to return to his work as a butcher. There was coincidental improvement in the electromyograph. In view of this good response the boy was then treated in the same way, with equally dramatic results. The actiology of this syndrome is quite obscure, but some aspects are discussed, including the "stiff-man" syndrome. It is concluded that the condition described is separate from the group of myotonic disorders. Hugh Garland

952. On the Function of the Endocrine Glands in Myotonic Muscular Dystrophy

W. D. DRUCKER, L. P. ROWLAND, K. STERLING, and N. P. CHRISTY. American Journal of Medicine [Amer. J. Med.] 31, 941-950, Dec., 1961. Bibliography.

Studies of endocrine function were carried out on 17 patients, aged between 28 and 68, suffering from dystrophia myotonica. The basal metabolic rate was found to be low in 11 of 15 patients, but isotope studies showed no evidence of hypothyroidism and the low basal metabolic rate remains unexplained. Adrenal cortical function was normal, as was also ovarian function. Testicular atrophy occurred in 7 out of 9 men, but previous to this 5 of the 6 married men had been fertile. From the present study and from a review of the literature it is concluded that there is no evidence of adrenal cortical, thyroid, ovarian, or pituitary deficiency in dystrophia myotonica. The incidence of diabetes mellitus is estimated to be about 18%. Hugh Garland

Psychiatry

953. An Investigation of Certain Factors Conditioning the Formation of the Psychopathies. (К исследованию некоторых факторов, обусловливающих становление психопатий)

V. Ja. GINDIKIN. Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1546–1554, No. 10, 1961. 34 refs.

This paper from the Professorial Department of Psychiatry, Institute of Medicine, Moscow, presents a study of those factors operating during the early years of life which seemed to be of basic importance in the development of psychopathy. Particular attention was paid to psychopathic inheritance, the material conditions of life, the character traits of the parents and their influence on upbringing, and the qualitative aspects of the upbringing in general. A series of 110 patients diagnosed as suffering from psychopathic personality in a state of decompensation were studied in hospital or as out-patients and 100 controls were chosen consisting of students, schoolboys, and men of various professions. All the reported differences between patients and controls were significant as tested by the χ^2 test. It was not found possible to group the patients according to any existing classification, nor was it desirable in view of the large number of groups which would each have contained only a few patients. However, they were divided roughly into four groups: (1) an excitable, irascible, irritable group; (2) an inhibited, asthenic, schizoid group; (3) a mixed group showing some features of both the first two; and (4) a hysterical group.

Investigation of the heredity of the patients was not an aim in itself, but simply a means of investigating the conditions of the patients' early years of life. Of 102 patients for whom information was available, 39 had a

history of psychiatric illness in the family.

About one-third of the patients had suffered adverse material conditions of life such as famine, destruction due to war and revolution, or hardship in connexion with alcoholism in the parents. There was no connexion between the severity of these adverse conditions and any of the groups of psychopathy except that they were rare among hysterics.

There was a significant preponderance of psychopathic personality traits among the parents of the patients as compared with the controls, but there was no regular relationship between the type of personality deviation in parent and child, a fact which leads the author to speak not of the inheritance of specific personality traits but rather of the inheritance of a certain instability of the nervous system. It was found that character deviation in the parent gave rise to irregular upbringing much more frequently in the psychopathic group than in the controls and this was thought to be due to the greater susceptibility of the psychopath to environmental influence. Those psychopaths who had an irregular up-

bringing generally had parents with marked psychopathic character traits, whereas this was the exception among members of the control group who had had an irregular upbringing. Irregular upbringing was much commoner in the psychopathic group and was to some extent independent of character deviation in the parents since the number of parents with normal personalities giving their children an unsatisfactory upbringing was also significantly greater in the psychopathic group. The main types of unsatisfactory upbringing were as follows: (a) too great demands put on the child; (b) ill-treatment and lack of affection; (c) neglect; and (d) spoiling. Neglect and ill-treatment were commoner in the psychopathic group and spoiling among the controls, the latter usually being associated with hysterical personality traits in the child. Among the psychopaths neglect was commoner among irritable patients, ill-treatment among the inhibited group, and spoiling among the hysterics.

The author recommends as a prophylactic measure that the children be reared away from psychopathic parents. He does not think that his results allow the certain conclusion that poor upbringing ever operates independently of pathological inheritance; he does, however, consider that it is a more important aetiological factor.

[The detailed statistical treatment of the data in this paper is at times vitiated by the presence of differences between the psychopathic and control groups for which no allowance is made. Thus while it was found that character deviation in the parents of the psychopathic group gave rise to irregular upbringing more often than in the controls, no allowance is made for the admittedly greater severity of character deviation in the parents of the psychopaths.]

G. P. McGovern

954. Remand Home Boys, 1930-1955

M. D. EILENBERG. British Journal of Criminology [Brit. J. Crim.] 2, 111-131, Oct., 1961. 34 refs.

This report, which is presented from the Maudsley Hospital, London, compares the results of intelligence testing and of physical examination of a random sample (244) of all the boys admitted to Stamford House Remand Home, London, in the year 1955 with similar data for a sample of the inmates of a remand home (or "place of detention", as it was then called) examined in 1930, and also with comparable data for ordinary school-children published by the London County Council (L.C.C.) in 1954.

Some features of these remand home boys have remained unchanged over the 25 years between the two studies. Thus in both samples 90% of the boys were retarded in educational attainment, but the degree of retardation was more marked in the 1955 sample, in which nearly one-half (48·2%) were retarded by 4 years or more. Analysis showed that the severer degrees of

retardation occurred more often in those who had been born just before or at the beginning of the last war, presumably because their education had been disturbed by evacuation from London and other events of the war. In the main the scholastic retardation was not due to low intelligence, since 39% of the 1955 sample had an I.Q. above the mean of 100, and there were fewer instances of definite subnormality (2.1%, compared with 7.5% in 1930). The offences leading to admission were substantially the same in 1955 as in 1930, theft forming the majority (66 and 58% respectively) and sexual offences a small minority (2.0 and 1.5% respectively). The range of articles stolen was also much the same, with the exception of motor vehicles, of which only 2 were stolen in 1930 compared with 22 in 1955. In both samples about half of the offences were committed by the boy when alone; the proportion of offences committed alone increased with age.

In regard to physique the boys in the 1955 group showed a marked greater height and weight at all age levels, and a very much smaller incidence of undernourishment than the 1930 series. However, their nutritional status was still somewhat under the average for the L.C.C. control group of normal children. They were also on average slightly heavier and slightly shorter than the controls. The chief difference from the L.C.C. group, however, was the higher incidence of minor physical disorders, such as skin diseases, ocular refractive errors, and ear, nose, and throat conditions, and the markedly higher incidence of enuresis—13.2% compared with 1.57%.

D. J. West

955. Visual Illusion, Tactile Sensibility and Reaction Time under LSD-25. [In English]

A. E. Edwards and S. Cohen. *Psychopharmacologia* [*Psychopharmacologia* (*Berlin*)] 2, 297-303, 1961. 9 refs.

One of the features described by most subjects who have received lysergic acid diethylamide (L.S.D.) has been the changes they experience in sensory function. These include increased brilliancy and colour saturation of the object viewed, together with an apparent enhancement of both depth and texture. Experiments by Abramson (J. Psychol. (Provincetown), 1955, 40, 39) suggested that these changes may result from a central impairment of sensory modalities. In the present study, reported from the Veterans Administration Center, Los Angeles, the changes in sensory perception and in performance of tasks were investigated in 15 subjects of average educational level who received 125 μ g. of L.S.D., their performance in a series of standardized tests being compared with their performance under non-drug conditions. The results of these tests showed that there was a general impairment of reaction time and skin sensitivity, but that colour detection was unchanged. The results are discussed and compared with those of other workers. No simple generalization appeared to explain the present findings, but it is suggested that a damping of "somaesthetic" sensations with a reduction in visual cues may account for many of the unusual subjective sensations reported by subjects receiving B. M. Davles L.S.D.

956. Effects of Lysergic Acid and Various Derivatives on Depth and Cortical Electrograms

R. R. MONROE and R. G. HEATH. Journal of Neuropsychiatry [J. Neuropsychiat.] 3, 75-82, Dec., 1961. 4 figs., 12 refs.

In a previous paper the authors reported finding subcortical paroxysmal electrographic activity in the septal and hippocampal regions in schizophrenic patients. In this paper from Tulane University School of Medicine, New Orleans, they describe the effect of lysergic acid derivatives on electrograms from animals with chronically implanted subcortical electrodes. The methods of implanting electrodes and the records obtained are described.

The authors' results appear to show that paroxysmal activity in the rhinencephalic structures correlates with disturbed behaviour in the animals produced by lysergic acid and mescaline. In animals which showed catatonic-like behaviour there were electrophysiological changes in the septal region, while if agitation and aggression occurred there was hypersynchronous activity in the hippocampal region. When no electrographic changes occurred there were no changes in behaviour.

B. M. Davies

957. Catamnestic Studies in Neurotics. (Катамнев больных неврозами)

E. K. JAKOVLEVA and R. A. ZAČEРІСКІІ. Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1529–1533, No. 10, 1961. 13 refs.

This paper presents a catamnestic study of 300 neurotic patients discharged from the Bekhterev Psychoneurological Institute, Leningrad, 10 to 25 years previously. Follow-up was carried out by means of personal interview of out-patients and hospitalized patients and also by questionaries given to the patients in their homes and places of work.

Of the 300 patients, at the time of discharge from hospital 120 (51.6%) were completely well and 69 (21.4%) showed permanent improvement. However, the percentage of recovery was different for the different forms of neurosis. Hysterical reactions showed recovery or permanent improvement in 92.6% of cases, whereas the figures for the other neuroses were: neurasthenia 74.4%. obsessional states 69.8%, psychasthenia 43.4%, and hysteria 32.8%. The absolute numbers of those suffering from psychasthenia and hysterical reactions were small. The authors stress the necessity for making a distinction between hysteria and hysterical reaction, the latter often having a favourable prognosis. Among the psychasthenics and hysterics who improved, incomplete recovery was the rule, whereas patients with hysterical reactions, obsessional states, and neurasthenia usually showed complete cure.

The follow-up data are presented in comparison with the condition of the patients on discharge from hospital. Of 218 patients discharged cured or improved, 114 remained well or maintained their improvement. Out of 148 of those patients who had only been improved on discharge, 49 were found at follow-up to be cured. The tendency towards subsequent cure or improvement was

most marked with neurasthenia and hysterical reactions. Detailed study of the histories showed that a favourable outcome was determined for the most part by psychotherapy continued on an out-patient basis and supplemented by work therapy. Improvement of the patient's conditions of work and life in general and the taking up of socially useful work also helped. A short duration and moderate severity of illness, especially as affecting the younger age groups, favoured a good outcome. Relapse or worsening was often associated with fresh psychic trauma, somatic or neurological illness, or, in women, the climacteric. The authors do not accept the views of certain Western authors that spontaneous cure of the neuroses is possible.

G. P. McGovern

958. A Comparison of Promazine and Paraldehyde in 175 Cases of Alcohol Withdrawal

W. T. HART. American Journal of Psychiatry [Amer. J. Psychiat.] 118, 323-327, Oct., 1961. 1 fig., 17 refs.

In a study at Monroe County Psychiatric Hospital Unit, Rochester, New York, 175 patients suffering from alcohol withdrawal syndromes were treated with promazine and paraldehyde, both separately and together, the duration of treatment being between one and 15 days. The criteria for definition of withdrawal syndromes were strictly adhered to, and the clinical state of the patients was charted by the doctors and nursing staff on the basis of 7 different symptoms. It was found that with promazine, 400 mg. per day, the duration of symptoms was shorter than with paraldehyde alone or with paraldehyde and promazine combined; for example, only 12% of the patients receiving promazine were anxious and agitated at the end of the 4th day, while for those given paraldehyde the proportion was 55%.

[While this investigation was carefully carried out, the fact that vitamin-B complex and multivitamins were administered to all patients for the first 3 days of their treatment makes it difficult to judge how much this may have contributed to the relief of symptoms.]

N. Rathod

AFFECTIVE DISORDERS

959. Salivation in Depressed Patients

G. GOTTLIEB and G. PAULSON. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 468-471, Nov., 1961. 5 refs.

At the Dorothea Dix Hospital, Raleigh, North Carolina, 18 in-patients (12 female and 6 male) suffering from depression were subjected to salivation tests before and after treatment; a control group consisting of 8 members of the hospital staff underwent similar salivation tests at 12 months' interval. Patients were diagnosed as suffering from "depressive reaction", "psychotic depression" or "involutional depression". On admission, and again after treatment when considered ready for discharge, patients were tested by a modified version of the depression scale of the Minnesota Multiphasic Personality Inventory. All patients showed a definite improvement in scores on this scale. During their illness the patients had a significantly lower saliva-

tion rate than had the controls. But even when their condition improved after treatment the patients' salivation rate had not altered significantly, and still remained lower than that in the controls. It is concluded that factors other than the degree of depression present at the time of testing are responsible for the lowered salivation rate in patients liable to suffer from depression.

E. H. Johnson

960. Studies of Salivation in Depression. II. Physiological Differentiation of Reactive and Endogenous Depression

B. L. Busfield Jr., H. Wechsler, and W. J. Barnum. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 472–477, Nov., 1961. 9 refs.

At the Massachusetts Mental Health Center, Boston, salivation rates were determined in 109 severely depressed patients from three State hospitals who were divided into two groups according to whether the depression was diagnosed as being exogenous or endogenous. The former group included psychoneurotic and psychotic depressive reactions, and depressions with personality disorder. Those without psychological and environmental determinants were classed as endogenous depression; on the basis of recurrence of the illness these patients appeared to have a biological tendency to depression. This group included the involutional and manic-depressive types.

Patients with endogenous depression were found to salivate at a lower rate than those with the exogenous type, and depressed female patients showed a lower salivation rate than depressed males, as did also elderly patients than the younger ones. Even after allowing for these factors, however, the endogenous patients still had a lower rate of salivation. It was also found that salivation rates were independent of the severity of the depression in all groups.

The symptom of "dry mouth" was also examined, but this was shown to bear no relation to the diagnostic category of the patient, or to the actual salivation rate.

E. H. Johnson

961. A Systemic Investigation of Depression

A. T. Beck. Comprehensive Psychiatry [Comprehens. Psychiat.] 2, 163-170, June [received Nov.], 1961. 1 fig., 6 refs.

The present report is one of a series designed to test the hypothesis that depressed patients have a persistent "need to suffer". The author describes the tendency to seek suffering as masochism, without implying any derived sexual gratification. Out-patients and in-patients of the Psychiatric Departments of the Hospital of the University of Pennsylvania and the Philadelphia General Hospital were subjected to a full clinical assessment (162 patients), an inventory designed to measure the depth of depression (226 patients), a projective test designed to elicit masochistic themes (87 patients), and an inventory containing items supposedly differentiating masochism, hostility, and submission (109 patients). Reports of the patient's most recent dream (219 patients) and of his three earliest memories (25 patients) were also rated for self-punitive content.

The author claims high reliability for the clinical assessments, and for the inventories. He reports that there was a high correlation between clinical rating of depression and scores on the inventory; that the most depressed group of patients had significantly more masochistic dreams than did the non-depressed group; and that there was a higher frequency of masochistic early memories and a higher score on the masochism inventory among the more depressed patients. R. H. Cawley

SCHIZOPHRENIA

962. Remissions in Schlzophrenics after Treatment with Neuroleptic Drugs and Maintenance Therapy. (О ремиссиях у больных шизофренией после лечения нейролептическими средствами и поддерживающей терапии)

G. V. ZENEVIČ. Журнал Невропатологиили Психиатрии [Ž. Nevropat. Psihiat.] 61, 1728–1734, No. 11, 1961. 26 refs.

The author draws attention to certain unsolved problems which arise during the maintenance therapy of schizophrenic patients with neuroleptic drugs, in particular the characteristics of the course of the illness during such therapy, the method of giving the drugs, and certain questions of organization. He presents some comparative data on 150 out-patient schizophrenics who were treated with a neuroleptic drug (usually chlorpromazine) and who were studied currently and retrospectively, and goes on to make some general observations and recommendations.

The results of treatment with chlorpromazine are compared with those obtained by other methods, mainly electric convulsion therapy (E.C.T.), the first figure in each case representing the results obtained with chlorpromazine: (1) well and practically recovered, 16 and 14% respectively; (2) remissions with slight residual symptoms 23.7 and 26.2%; (3) remissions with pronounced residual symptoms 41.3 and 23.2%; (4) defect states 20 and 26.4%. Of the chlorpromazine-treated group 11.3% had to be admitted once and 40% on more than 4 occasions, in comparison with 40% and 11.4% for the other group. The E.C.T.-treated group contained more patients who had returned to normal work, but this was balanced by more doing no work at all. Although patients who responded well to the neuroleptic drug often continued to improve, yet more of them relapsed than among the shock-treated group, and also they often remained at a lower level of adaptation after 'treatment of the relapse. Nonetheless, many patients who relapsed responded promptly to an increased dosage of chlorpromazine.

The author found it impossible to predict which cases would continue to require maintenance drug therapy or to account for the observed differences, except that he considers that cases previously achieving spontaneous remission have a more favourable prognosis. Symptoms such as apathy, hypochondriasis, and asthenia may persist even after withdrawal of the drug. He recommends that the drug should always be withdrawn by gradual

reduction of dosage, followed by prompt increase of dosage at the first sign of relapse. In his experience a positive role is played by stimulants, tonics, antidepressive drugs, work therapy, psychotherapy, and spells of rest from work. At the present time in Russia the hospitals in which schizophrenic patients are treated and the climics in which they are seen subsequently for follow-up are separately staffed and a plea is made for closer liaison between the two centres.

G. P. McGovern

963. Preliminary Studies on Peripheral Glucose Metabolism in Schizophrenia

J. K. McDonald. Journal of Neuropsychiatry [J. Neuropsychiat.] 3, 23-27, Oct., 1961. 2 figs., 22 refs.

In most previous studies dealing with glucose metabolism in schizophrenia glucose levels have been measured in venous blood and little attention has been paid to peripheral glucose utilization, as reflected by arteriovenous glucose differences. These earlier studies have indicated that there is a defect in glucose metabolism in schizophrenia due to a "plasma factor". The present paper, from the Medical College of Georgia, Augusta, describes the effects of insulin, glucagon, adrenaline, and "stress" on changes in the arterio-venous difference in glucose levels in the brachial or radial artery and antecubital vein of 18 schizophrenic patients. After the intravenous infusion of insulin and glucagon there was an increase in peripheral glucose utilization. After adrenaline the response showed an unexpected increase in glucose utilization, while with "stress" there was a fall in peripheral glucose utilization. This last finding is important and in the author's view needs to be further studied both in patients with schizophrenia and in normal subjects, since Gottlieb has suggested that in schizophrenic patients the defect in utilizing glucose may not operate or may become apparent only during periods of B. M. Daples

964. Reappraisal of Biological Aspects of Psychiatry R. H. HEATH. Journal of Neuropsychiatry [J. Neuropsychiat.] 3, 1-11, Oct., 1961. 9 figs., 18 refs.

This paper from Tulane University School of Medicine, New Orleans, emphasizes the basic biological disease process in schizophrenia. The author reviews his earlier work in which he studied the relationship between fluctuations in subcortical and cortical function on the one hand and changes of behaviour on the other. This was made possible by means of the precise implantation of electrodes in various regions of the brain; these were left in position for periods of several months up to 2 years in patients suffering from a variety of behavioural disorders, as well as in a small number of normal volunteer subjects.

The most significant finding has been the correlation between changes recorded from the septal region and the hippocampus with fluctuations in the patient's behaviour. In schizophrenic patients such recorded changes included a large spike and slow wave localized to these regions, the abnormalities disappearing when the patient's condition improved. Taese findings were present in all of the 39 schizophrenic patients studied in this

way and were absent in the healthy control subjects. When the specific serum fraction (taraxein) which was isolated from the serum of schizophrenic patients was given to monkeys or non-psychotic human subjects, similar electrical changes occurred and were accompanied by schizophrenic behaviour.

[While this important work needs corroboration by other investigators, it does show some of the ways in

which mental illness can now be studied.]

B. M. Davies

TREATMENT

965. The Psycho-active Drug 7162 RP (Dimethyl-amino-3'-methyl-2'-propyl)-5 Immodibenzyl. Therapeutic, Panpsychotropic, and Analgesic Properties. (Le,psycho-actif, 7162 RP (dimethylamino-3'-methyl-2'-propyl)-5 immodibenzyle). Propriétés thérapeutiques, panpsychotropes et anti-algiques)

J. SIGWALD, D. BOUTTIER, P. RAVERDY, C. RAYMON-DEAUD, P. PERRIER, and J. L. DONNET. Presse médicale [Presse méd.] 69, 1780-1783, Oct. 7, 1961.

7162 RP is a new drug structurally related to imipramine ("tofranil") by its iminodibenzyl nucleus and to levomepromazine ("veractil") by its dimethylaminopropyl side-chain. This dual relationship, it is claimed, is reflected in its therapeutic range. Thus 7162 RP, like chlorprothixene ("taractan"), merits the description "panpsychotropic". The authors have treated 113 patients (some ambulant and some in hospital) with 7162 RP in daily doses of 125 to 800 mg, given orally for periods up to 6 months. The psychiatric cases included 82 patients with neuroses of all kinds, 19 with various depressive syndromes, and 2 with hallucinatory psychoses. The drug was also given to 19 neurological patients of whom 7 had the post-concussion syndrome and 12 had various neuralgias. Beneficial results were obtained in every condition studied in approximately 80% of the

The principal side-effects were a tremor of mixed type and a bucco-facial weakness with dysarthria. No toxic effects were seen.

[This study was uncontrolled and therefore does not permit of any conclusions being drawn about the role of 7162 RP in rational therapy.]

B. S. Meldrum

966. The Intermittent Administration of Neuroleptics, with Special Reference to Thioproperazine. (De l'administration intermittente des neuroleptiques notamment de la thiopropérazine)

G. DESHAIES and P. BENDA. Presse médicale [Presse méd.] 69, 2297-2299, Nov. 25, 1961. 6 refs.

This paper describes the experience gained in treating 156 patients with acute and chronic psychoses with intermittent doses of thioproperazine methanesulphonate ("majeptil"), a new phenothiazine derivative. The drug was given in a single large dose of between 30 and 80 mg., either in the morning or at night and repeated two or three times per week, so that treatment days alternated with days when no drug was given. Toxic side-effects were maximum 7 hours after administration

and took the form of frequent excitomotor crises, which in 10% of cases were severe. After a time these signs gradually waned. The progress of these symptoms and the effective changes associated especially with the recovery phase were thought to stimulate a closer relationship between the patient and his environment, while at the same time psychotherapy was believed to be facilitated.

The 156 patients included schizophrenics and other chronic deteriorated patients, many with depressive and anxiety states. Of the chronic psychotic group, which included schizophrenics and others, 25% were discharged from hospital as the result of treatment. Of those with acute confusional states the discharge rate amounted to 80%. Hypomanic patients were only partially helped.

The authors compare the subjective effects of thioproperazine and those of such drugs as lysergic acid diethylamide. On the practical side the ease of administration and manageability of the patients were further advantages of this new drug.

J. S., Bearcroft

967. Clinical Experience with Psilocybin. (Klinische Erfahrungen mit Psilocybin)

M. SERCL, J. KOVARIK, and O. JAROS. Psychiatria et neurologia [Psychiat. et Neurol. (Basel)] 142, 137-146, 1961. 16 refs.

Psilocybin is a new "psycholytic" drug which has been isolated from the Mexican fungus *Psilocybe mexicana* Heim. Before testing the therapeutic value of the new drug the authors examined its effect on healthy persons and found that an oral dose of 1 to 2 mg. produced euphoria, facial hyperaemia, and mydriasis in 4 out of 5 subjects. Subcutaneous injections of 3 to 6 mg. had similar results in 7 out of 10 subjects; in the 3 remaining subjects in this group unpleasant side-effects occurred which were, however, accompanied by "euphoric thoughts".

Of 15 neurological patients, suffering variously from disseminated sclerosis, polyneuritis, or post-encephalitic conditions, who complained of secondary depressive symptoms, 6 reacted with definite euphoria, an increase in the tendon and pilomotor reflexes, slight mydriasis, and heightened dermographism. Of 15 patients with reactive and endogenous depression, all responded with euphoria. All the patients received a placebo one day without their knowledge and on that day only 6 patients reported a euphoric mood. The effect of the drug was shown to begin after 15 to 30 minutes and to last for 3 to 5 hours. The euphoric effect produced by it facilitated psychotherapy. Treatment with the drug could be discontinued after 10 days without the occurrence of withdrawal symptoms or signs of tolerance or addiction. Side-effects, which were rare and mainly occurred after administration by subcutaneous injection, consisted in brief facial hyperaemia, a feeling of "pressure at the back of the head", and disturbance of concentration. It is stated that other workers who had given daily doses higher than 1 to 2 mg. by mouth or 3 mg. subcutaneously have reported a higher incidence of side-effects.

F. K. Taylor .

Dermatology

968. Controlled Trials of Two Oral Antipruritic Drugs, Trimeprazine and Methdilazine

M. A. SMITH and M. P. CURWEN. British Journal of Dermatology [Brit. J. Derm.] 73, 351-358, Oct., 1961. 2 figs.. 5 refs.

These controlled clinical trials of trimeprazine tartrate and of methdilazine hydrochloride in the symptomatic treatment of chronic pruritus were carried out at St. Bartholomew's Hospital, London. It is concluded that both drugs have a real antipruritic effect, although the proportion of patients likely to benefit may not be more than one-quarter. Drowsiness, which was the chief side-effect of both drugs, occurred in about one-third of the patients. There were no other complications. Most of the patients had some form of eczema.

E. W. Prosser Thomas

969. The Treatment of Chronic Discold Lupus Erythematosus with a Combination of Antimalarial and Corticosteroid Drugs

S. ALEXANDER and M. A. COWAN. British Journal of Dermatology [Brit. J. Derm.] 73, 359-361, Oct., 1961.

Most patients with chronic discoid lupus erythematosus respond well to antimalarial drugs, but there is a "hard core" of about 20% in whom some disease activity persists. The authors of this paper from the Radcliffe Infirmary, Oxford, describe the results obtained with either triamcinolone or prednisolone as well as an antimalarial drug in 11 patients who had not responded satisfactorily to previous treatment. In all 11 patients there was complete control of disease activity within a month of starting the combined treatment. Side-effects were encountered in 3 patients receiving triamcinolone—weakness and lassitude in one patient and thrombophlebitis in 2; in one of the last 2 patients bilateral rupture of the tendo achillis subsequently developed.

E. W. Prosser Thomas

970. An Association between Bowen's Disease and Internal Cancer

E. S. PETERKA, F. W. LYNCH, and R. W. GOLTZ. Archives of Dermatology [Arch. Derm.] 84, 623-629, Oct., 1961. 17 refs.

In 1959 Graham and Helwig (A.M.A. Arch. Derm., 80, 133; Abstr. Wld Med., 1960, 27, 239) reported a possible relationship between Bowen's disease of the skin and visceral cancer. The authors have therefore undertaken this follow-up study of all (74) patients with Bowen's disease seen at the University of Minnesota Hospitals, Minneapolis, between 1941 and 1955; adequate follow-up information was obtained for 53 of these. Because of the histological difficulty of differentiating senile keratosis from Bowenoid dyskeratosis the cases were divided into two groups consisting of (1) 33 patients (21 male and 12 female) in whom the lesion occurred on a covered area of the body, and (2) 20 patients

(8 male and 12 female) in whom the lesion was on an exposed area.

Of the 33 patients in Group 1 (median age 70 years) 16 had died, 7 having had internal malignant disease which developed on the average 6 years after the initial diagnosis, while of the 17 still living 4 others had internal malignancy which also developed at an average of 6 years after the diagnosis of Bowen's disease. Of the 20 patients in Group 2 (median age 71) no evidence of malignancy was found in the 10 patients still living and there was only one case of internal malignancy among the 10 who had died. It is noted that 11 of the patients in Group 1 and 6 of those in Group 2 developed other cutaneous cancers. The authors consider that there is a significant association between internal cancer and Bowen's disease, particularly when the cutaneous lesion appears on an unexposed area of the skin. They suggest that careful follow-up of patients with Bowen's disease might contribute to the early recognition of asymptomatic internal cancer. Benjamin Schwartz

971. Treatment of Lupus Vulgaris with INH, PAS, and Tebamine. [In English]

R. A. Wehnert and P. V. Marcussen. Acta dermatovenereologica [Acta derm.-venereol. (Stockh.)] 41, 461-470, 1961. 1 fig., 31 refs.

In this paper from the Finsen Institute, Copenhagen, a trial is reported of isoniazid with and without PAS or "tebamine" (para-aminosalicylic acid phenyl ester) in the treatment of 168 cases of lupus vulgaris, treatment being given for a minimum of one course to a total of 4 courses if recurrences demanded it. Regardless of body weight isoniazid was administered in a dosage of 300 mg. daily. Follow-up examinations were carried out at 3-to 6-month intervals during the first 2 years and annually thereafter. At the 5-year follow-up 154 patients were cured; 13 patients did not, for various reasons, complete the treatment and in one patient tubercle bacilli became resistant to isoniazid.

The total dose of isoniazid administered in a course varied from 18 g. to 120 g. The results obtained with repeat courses of a smaller dosage of the drug were not as good as those obtained with a single continuous course of the same total dosage. It is suggested that with intermittent treatment "patients develop a relative resistance". The best results were obtained with a course of 120 g. administered over 400 days.

During the first year there were 30 recurrences; during the second 13, during the third 7, and during the fourth 2; in the fifth year there were no recurrences. The cure rate at the 5-year follow-up was 92%. The addition of PAS or tebamine to the treatment regimen had no significant effect. The authors point out, however, that since other forms of tuberculosis, pulmonary or extra-pulmonary, are common in patients with lupus vulgaris it is advisable to give the combined treatment. In one

patient in the series treatment with isoniazid had to be discontinued because of side-effects of the drug. It is stated that gastro-intestinal side-effects of PAS can be controlled with tebamine. Cultures from biopsy specimens taken before treatment or during a recurrence were positive for tubercle bacilli in 70% of cases.

E. H. Johnson

P72. The Etiology and Treatment of Erythrasma
 I. SARKANY, D. TAPLIN, and H. BLANK. Journal of Investigative Dermatology [J. invest. Derm.] 37, 283-290, Oct., 1961. 6 figs., 11 refs.

Writing from the University of Miami School of Medicine, Florida, the authors state that erythrasma, first described by Burchardt in 1859, is much more common than is generally supposed since 22% of 107 subjects selected at random showed evidence of the infection in their toe webs. Scales of erythrasma always contain Gram-positive rods and/or filaments with granules, and a red fluorescence is seen in the lesions viewed under Wood's light and also in the colonies of bacteria obtained from the scales.

Electronmicrographic studies of the cultured organisms confirmed that they are bacteria containing electrondense granular elements. A Gram-stained smear from a colony showed Gram-positive rods 1 to 2μ in length and 0.3 to 0.6μ wide, with a tendency to become pleomorphic and Gram-negative in older cultures. Five experimental inoculations of pure cultures into 4 human subjects resulted in 3 positive reactions. Scaly lesions were produced which showed red fluorescence within 72 hours, but the lesions faded within a day or two and failed to persist as clinical erythrasma. Further evidence of the bacterial nature of the condition was afforded by the rapid response to antibacterial antibiotics given systemically-particularly to erythromycin in a dosage of 1 g. daily for 5 days. Chloramphenicol and the tetracyclines were also effective, but penicillin and griseofulvin were ineffective. Erythromycin and chloramphenicol given topically did not clear the lesions completely. These tests were carried out on 15 affected patients.

R. R. Willcox

973. Erythema Nodosum. A Review of One Hundred and Fifteen Cases

H. GORDON. British Journal of Dermatology [Brit. J. Derm.] 73, 393-409, Nov., 1961. 41 refs.

Following a review of some of the literature relating to the association of erythema nodosum with tuberculosis, streptococcal infection, drug reactions, hilar lymph node enlargement, sarcoidosis, and a variety of other conditions, the author presents the results of a follow-up investigation of all (115) cases of erythema nodosum admitted to the Newsham General Hospital, Liverpool, in the years 1948 to 1958, representing 0.91% of the total number of admissions. Of these patients 102 (88.7%) were female and 13 (11.3%) males, and the maximum incidence was in the age group 15 to 24 years. In 19 patients tuberculosis was present at the time of the skin lesions or appeared shortly afterwards, 3 others developed tuberculosis subsequently, and 2 further cases were classed as suspected tuberculosis (20.9% in all).

In 9 cases (7.8%) the disease was considered to be associated with streptococcal infection, while 15 patients (13%), including one known to have sarcoid, showed hilar lymphnode enlargement. In a miscellaneous group of 13 patients (11.3%) there was a possible association with pregnancy in 3, hypochromic anaemia in 2, chronic bronchitis in 3, and in 1 case each with herpes, mild rheumatoid arthritis, gingivitis, and partial atelectasis of the middle lobe of one lung; one patient subsequently developed Crohn's disease. However, no disease was found apart from the skin lesions in the remaining 54 patients (47%).

Tuberculosis, in spite of its general decline in incidence, still appears to be the most common single disease associated with erythema nodosum and the author recommends that follow-up chest radiographs for 2 years should be obtained in all cases, together with investigation of the patient's contacts for latent tuberculosis.

Benjamin Schwartz

974. Treatment of Psoriasis with Mercaptopurine R. E. KRAVETZ and T. BALSAM. Archives of Dermatology [Arch. Derm.] 84, 597-600, Oct., 1961. 1 fig., 10 refs.

The use of the antimetabolite aminopterin has been shown to be of value in the treatment of psoriasis, but the appearance of secondary toxic manifestations following use of the drug in a dosage high enough to be effective has precluded its general acceptance. In this report from the Veterans Administration Hospital, Brooklyn, New York, the authors describe their treatment of psoriasis with another antimetabolite, mercaptopurine, which is said to interfere with nucleic acid biosynthesis. In all, 12 adult male patients with refractory psoriasis were treated between July, 1959, and November, 1960, the drug being given orally in a dosage of 2 mg. per kg. body weight daily in divided doses, the total daily dose usually being between 150 and 250 mg. Careful watch was kept for signs of toxicity; the occurrence of nausea, vomiting, diarrhoea, ulceration of membranes, or signs, of bone marrow depression was considered sufficient reason for suspension of treatment. In all, 24 courses of treatment were given, their duration varying from 14 to 62 days (average 32 days).

The results were considered to be good to excellent in 16 of the 24 courses. Clinical improvement was noted as early as 7 to 10 days after the beginning of treatment, but there was no correlation between the degree of clinical improvement and the total dosage given. Only one course was complicated by nausea and vomiting, but in 10 patients there was a depression of 50% or more of the formed elements in the peripheral blood. The blood changes reversed when treatment was discontinued; there appeared to be no association between such changes and the total dosage of mercaptopurine given. No prediction could be made regarding the response to one particular course on the basis of previous responsiveness, nor was it possible to predict the length of a remission in cases in which the disease had recurred, having been -previously responsive. The authors conclude that mercaptopurine may be used under close supervision on an experimental basis in refractory cases of psoriasis:

Benjamin Schwartz

Paediatrics

975. The Protein Allowance in Infancy and Childhood J. A. Johnston, M. J. Sweeney, R. C. Brown, J. W. Maroney, and G. Manson. *Journal of Pediatrics [J. Pediat.]* 59, 47–55, July, 1961. 1 fig., 18 refs.

This complicated, yet incomplete, study of 31 male infants aged 9 to 75 days consisted of nitrogen balance studies at 2-weekly intervals after ad libitum intake of various dietary formulae each for 2 weeks. Gain in weight was greatest with a formula in which only 8% of calories came from protein, but increased retention of nitrogen was observed when the protein content of the formula was increased to 13%. No significant further increase occurred when higher-protein formulae were given up to 20% of total calories, but still higher nitrogen retention was found when 25% of the calories in the formula were derived from protein, and this was associated with loss of weight. These infants were apathetic and often refused feeds, and in retrospect the authors suggest that they were suffering from azotaemia or hyperelectrolytaemia. Margaret D. Baber

NEONATAL DISORDERS

976. The Fibrinolytic Enzyme Defect of Hyaline Membrane Disease

J. LIEBERMAN and F. KELLOGG. California Medicine [Calif. Med.] 95, 278-282, Nov., 1961. 2 figs., 21 refs.

The fibrinolytic enzyme system of 31 newborn infants who died from hyaline membrane disease has been studied at the University of California Medical Center, Los Angeles. Fibrinolytic activity was absent in 26 of these infants, whereas in a previous study such activity was shown to be present in 90% of newborn infants who died without evidence of hyaline membrane formation. The fibrinolytic enzyme defect was found to be due to an inhibitor which prevented the normal action of plasminogen activator, and the placentae of these infants were shown to contain this fibrinolytic inhibitor. It is therefore postulated that hvaline membrane disease is caused by the production of a fibrinolytic inhibitor from an infarcted placenta and that this inhibitor encourages the deposition of fibrin, a substance which arises from capillary exudate but which is normally removed by the action of fibrinolytic enzymes. R. M. Todd

977. Pulmonary Hyaline Membrane Disease: Origin in Premature Infants Delivered by Cesarean Section during Labor of after Placenta Previa or Abruptio Placentae F. F. SNYDER. Obstetrics and Gynecology [Obstet. and Gynec.] 18, 677-694, Dec., 1961. 11 figs., 31 refs.

Histological changes in the lungs of 41 premature infants who were delivered by caesarean section during labour or following antepartum haemorrhage were

studied at the Lying-in Hospital, Boston, Massachusetts. The presence of blood, epithelial cells, and debris in the foetal air passages was the most striking feature in the 5 stillborn and 36 live-born infants studied. Caesarean section in the 5 stillbirths was undertaken for abruptio placentae (3), prolapsed cord (1), and uterine inertia (1), and histological findings consisted in contamination of alveoli and bronchioles with blood in such amount that few air spaces were free of erythrocytes; no eosinophilic membrane could be detected.

In 20 of the 36 live-born infants delivered by caesarean section for placenta praevia contamination of air passages with blood was present, being marked in 9, and there was extensive lining of the walls of the alveoli and bronchioles with amorphous hyaline material in 18. Of 9 infants delivered by caesarean section for abruptio placentae, erythrocytes obstructed the air passages in 6, smaller accumulations of erythrocytes were seen in 3, and hyaline eosinophilic matter was widely distributed along the walls of the alveoli and bronchioles in 5. The indications for caesarean section in the remaining cases were uterine inertia (2), prolapsed cord (1), previous section (2), not stated (2); and histological examination of the lungs revealed erythrocytes widely distributed in the air spaces, with eosinophilic amorphous matter in the alveoli and bronchioles.

Thus no hyaline material was seen in 5 stillborn infants, but it was present in 83% of live-born infants; the suggested explanation is that, following alveolar expansion with air, any foreign material in the bronchi will be distributed in layers along the alveolar and bronchiolar walls.

Similar changes were found in a further group of 29 mature babies who died after caesarean section performed during labour or after antepartum haemorrhage. Erythrocytes were scattered in the alveoli and bronchioles in 28 of these babies. A little hyaline formation was seen in 7 babies who died within 3 hours of birth, but extensive hyaline material was present in 13 of 22 infants who died within 3 days of birth.

The author, disagreeing with the present majority view, considers that the fibrin-containing hyaline membrane is formed from inhaled material rather than from papillary exudation.

R. M. Todd

978. Prevention of Hyalin-membrane Disease in the Term Cesarean-section Infant

R. C. WRIGHT. Obstetrics and Gynecology [Obstet. and Gynec.] 18, 695-700, Dec., 1961. 2 figs., 10 refs.

This report from the New Britain (Connecticult) General Hospital is concerned with measures which can be taken to prevent inhalation of amniotic fluid by full-term infants born by caesarean section. It is customary after caesarean section to place the baby in the head-down supine position; in this position amniotic fluid

accumulates in the posterior pharynx and may be aspirated into the lungs with the first gasp. The author recommends that the baby be placed in the head-down prone position, with the obstetrician's finger in the baby's mouth, so that amniotic fluid will drain even from the posterior pharynx and pulmonary aspiration cannot occur. It is pointed out that the presentation of most babies born vaginally is occipito-anterior, so the baby emerges in the head-down prone position.

The author holds the view that hyaline membrane formation results from the interaction of plasma proteins from the pulmonary circulation with thromboplastin and acid mucopolysaccharides in the aspirated amniotic fluid; on this assumption hyaline membrane formation would be largely prevented if amniotic fluid was not aspirated.

[Only 2 short case records are given, and a larger trial will be necessary before this approach to the prevention of hyaline membrane can be evaluated.]

R. M. Todd

979. Thrush in the Newborn

H. SHRAND. British Medical Journal [Brlt. med. J.] 1530-1533, Dec. 9, 1961. 24 refs.

Thrush is often regarded as a mild and uncommon condition in the newborn; in this paper from Queen Charlotte's Maternity Hospital, London, it is shown to be commoner and potentially more serious than is generally held. During the period 1955-9 monilial vulvovaginitis was found in 232 mothers, an incidence of 1.5% of 14,873 live births. Whereas thrush occurred in the infants of only 0.5% of mothers without moniliasis, it was present in 77% of babies of mothers with moniliasis which had not been treated and in 2% where treatment had been adequate. The later monilial vulvovaginitis occurs in pregnancy, the more likely does it appear to influence the incidence of infection in the newborn infant, suggesting that the infant becomes contaminated in transit through the infected vagina. Previous authors have demonstrated other sources of infection: nurses' hands, utensils, and milk; and in the present series 5 infants born by caesarean section were affected. Prematurity, breast and bottle feeding, antibiotics, and the pH of the baby's mouth were not found to be predisposing factors. In treatment 3 to 4 drops of an aqueous solution of 0.5% gentian violet applied under the tongue after each feed was successful in most cases, and in the few which did not respond a suspension of nystatin, 100,000 units per ml., administered 4 to 5 times a day proved effective. David Morris

980. Familial Incidence of Infantile Hypertrophic Pyloric Stenosis. (Zum familiären Vorkommen der hypertrophischen Pylorusstenose des Säuglings)

J. GÖTZ and K. BETKE. Archiv für Kinderheilkunde [Arch. Kinderheilk.] 165, 16-27, Nov., 1961. 3 figs., 27 refs.

Of 367 children with pyloric stenosis seen at the University Paediatric Clinic, Freiburg, 44 came from families with a history of pyloric stenosis in other members (though it is noted that as it was not possible to be

certain of the diagnosis in all the relatives this figure is possibly a little too high). In 10 instances the parents had been affected, 2 mothers produced 4 children with stenosis, while 8 fathers had 13 affected children. In 12 cases at least 3 relatives had been affected. In one large family all 16 children had the condition and survived. Among the authors' 367 patients the ratio of boys to girls was 4 to 1, whereas in the families with affected relatives this ratio was only 2 1 to 1. The age of onset and cause of the disease appeared to be similar in all the children.

J. G. Jamieson

981. Sclerema Neonatorum Treated with Corticosteroids S. E. Levin, C. M. Bakst, and L. Isserow. *British Medical Journal [Brit. med. J.]* 2, 1533–1536, Dec. 9, 1961. 16 refs.

Cold injury in the newborn (sclerema neonatorum) is of common occurrence among the African population served by the Baragwanath Hospital, Johannesburg, and the authors of this paper have collected 25 cases over a 9-month period. As they were unable to trace in the English literature more than 17 cases of the disease treated with corticosteroids they set out to evaluate this form of treatment.

The sclerema was extensive in all but 5 infants, and all were warmed on admission, given oxygen for cyanotic attacks, and rehydrated intravenously when necessary. Although the plan was to administer corticosteroids to alternate babies, this was not achieved; antibiotics were given as indicated, and 11 patients received steroids, the other 14 acting as controls. The corticosteroid-treated group were all premature infants weighing at birth between 2 lb. 6½ oz. (1,091 g.) and 4 lb. 15½ oz. (2,254 g.); they were given an initial dose of 50 mg. of hydrocortisone intramuscularly followed by 25 mg. intramuscularly every 8 to 12 hours for up to 5 days. All but one infant died, and of the 5 cases in which necropsy was performed, pathological pulmonary changes were found in each. Of the 14 infants not given corticosteroids, 10 were prematurely born and weighed 2 lb. 2 oz. (964 g.) to 4 lb. 13 oz. (2,182 g.) (6 less than 3 lb. or 1,360 g.) at birth. Eleven of these infants died, and at the 2 necropsies pathological pulmonary changes were again found. Brief case histories of the 3 survivors are given.

The 2 groups were well matched for birth weight and the extent of the sclerema. The administration of corticosteroids seemed to make no difference to the outcome, the prognosis being apparently more influenced by the degree of the sclerema and the maturity of the infant.

David Morris

982. Haemolytic Disease of the Newborn. Control of Replacement of the Erythrocytes by Means of Foetal Haemoglobin

K. POLAČEK and M. HAJEK. Review of Czechoslovak Medicine [Rev. Czech. Med.] 7, 263-270, 1961. 8 refs.

In the treatment of haemolytic disease of the newborn the clinical results of exchange transfusion are usually satisfactory when the volume exchanged is 2 to 3 times the infant's blood volume. In difficult cases—for example, when complicated by severe anaemia and heart failure—a more accurate estimate of the volume to be exchanged is needed. The authors, at the Institute for the Care of Mother and Child, Prague, measured the decrease in foetal haemoglobin during 65 exchange transfusions, using an alkali denaturation precipitation method. Their results showed an exponential relationship between the removal of foetal haemoglobin and the volume of blood removed. They conclude that the optimum volume to be exchanged is 160 to 170 ml. per kg. body weight; exchange of a greater amount has little added value, while less than 140 ml. per kg. is not enough. In anaemic infants a smaller amount (100 to 140 mg. per kg.) is adequate.

F. P. Hudson

983. An Outbreak of Neonatal Deaths among Term Infants Associated with Administration of Chloramphenicol H. Lischner, S. J. Seligman, A. Krammer, and A. H. Parmelee Jr. *Journal of Pediatrics* [J. Pediat.] 59, 21–34, July, 1961. 3 figs., 41 refs.

This paper reports an investigation of the cause of death of 9 full-term infants occurring over a 2-month period in the newborn nursery of the University of California Medical Center, Los Angeles. All the infants died suddenly with symptoms of circulatory failure present for only 2 to 17 hours. All had received relatively large doses of chloramphenicol for prophylaxis or treatment of suspected infection, but the fatal outcome was unexpected and no adequate pathological cause of death was found at necropsy. A retrospective survey of antibiotic therapy over a 3½-year period strongly suggested that death was due to chloramphenicol in doses higher than usual. The literature relating to chloramphenical toxicity in the newborn is reviewed and the fact that manifestations are protean is stressed. The mechanism is unknown, but may be related to impaired glucuronide conjugation and diminished excretion.

Margaret D. Baber

CLINICAL PAEDIATRICS

984. Comparison of Fluoxymesterone and Methyltestosterone as Growth Stimulants

W. J. MELLMAN, A. M. BONGIOVANNI, M. GARRISON, and D. D. STEIKER. *Pediatrics* [*Pediatrics*] 28, 525–530, Oct., 1961. 5 refs.

The use of androgens as growth stimulants has the grave disadvantage of causing virilization and disproportionate epiphysial maturation. In order to evaluate the halogenated androgenic steroid fluoxymesterone, thought to be perhaps less disadvantageous, a double-blind controlled study was carried out at the Children's Hospital, Philadelphia, on 17 retarded children (14 of them boys) ranging in age between 7 and 13 years, who were divided into three comparable groups receiving respectively fluoxymesterone (2 mg. daily), methyltestosterone (10 mg. daily), and a placebo. The study extended over a one-year period consisting of 6 months of daily medication and 6 months' observation after treatment.

There was a significantly greater increment in height and bone age in the two groups receiving androgens than in the placebo group, bone age being accelerated to a greater degree than height increase, as in previous similar studies. No difference in testicular size was noted in the 3 groups but there was an increase in penile length in the treated subjects. The urinary excretion of 17-keto-steroids, oestrogens, and corticoids showed no consistent change, nor did the erythrocyte and leucocyte counts or the haemoglobin value vary significantly throughout the study. The serum calcium and phosphorus levels remained constant, but the mean serum alkaline phosphatase values were higher in the two treatment groups and remained so. The authors conclude that fluoxymesterone does not appear to offer any advantage over other derivatives of testosterone.

David Morris

985. Congenital Malformations. [Review-Article] J. WARKANY and H. KALTER. New England Journal of Medicine [New Engl. J. Med.] 265, 993-1001, Nov. 16, 1961, and 1046-1052, Nov. 23, 1961. Bibliography.

986. Therapeutic Trials in Phenylketonuria. (Essais therapeutiques dans la phenylcetonurie)
P. MOZZICONACCI, J. TREMOLIÈRES, C. ATTAL, F. GIRARD, R. LELUC, and J. BOISSE. Archives françaises de pédiatrie [Arch. franç. Pédiat.] 18, 569–602, May [received Nov.], 1961. Bibliography.

The authors first recall the metabolic abnormality which results in phenylketonuria, and then report their experience at the Hôpital Bicêtre, Paris, in treating the condition with a diet low in phenylalanine. They also describe an attempt to prevent mental deterioration in such patients by means of various other forms of treatment. The phenylalanine-poor diet was based on "ketonil", a proprietary casein hydrolysate containing 62% of protein and less than 0.1% of phenylalanine; fat was given in the form of arachis oil or butter, and carbohydrate in the form of saccharose and cornflour.

One child suffering from phenylketonuria was started on the diet at the age of 13 months; during the first few months of treatment an encouraging response was obtained, as judged by near-normal growth, remarkable improvement in his neuro-psychological condition, disappearance of phenylpyruvic acid from the urine, and normal level of serum phenylalanine during most of the period. However, symptoms of hypoproteinaemia occurred when ketonil was replaced by a synthetic mixture of 7 essential amino-acids, but improvement once more occurred when ketonil was again administered. At the end of 22 months of dietary treatment, however, the I.Q. was only slightly improved. In a further 2 cases the diet based on ketonil was tried for a short period in 2 children aged 11 and 8 years respectively. Phenylpyruvic acid soon disappeared from the urine and the serum phenylalanine level fell to 5 and 8 mg. per 100 ml. respectively. An improvement in behaviour was observed in the second of these 2 children, but gastrointestinal symptoms were troublesome while they were taking the diet.

Having regard to the fact that in phenylketonuria there is a deficiency of 5-hydroxytryptamine (5-HT; serotonin) owing to the abnormal metabolism of tryptophan, various other substances were investigated with a view to effecting an improvement by raising the level of cerebral serotonin. These included tryptophan and 5hydroxytryptophan (5-HTP), the precursors of serotonin; pyridoxine, which acts as a co-enzyme in the conversion of 5-HTP into 5-HT; and "marplan", which has an inhibiting effect on the amine oxidase enzyme which reacts with 5-HT. The drugs were given for short periods to 2 children, aged 21 months and 3 years, in the following dosage: DL-tryptophan alone in a dosage of 3 g. daily, the same drug combined with marplan in a dosage of 10 mg. daily, and pyridoxine in a dosage of 250 mg. daily. Although a review of the cases at the end of treatment showed little if any objective improvement, the authors consider that some of the clinical and biochemical effects obtained during treatment appear to justify further investigation on these lines.

Joseph Parness_

987. The Problem of Ketonaemia ("Acetonaemic Vomiting") in Childhood. Clinical and Experimental Studies. I. Symptomatology of Periodic Vomiting with Ketonaemia. (Das Ketonaemieproblem im Kindesalter ("acetonaemisches Erbrechen"). Klinische und experimentelle Untersuchungen. I. Zur Symptomatologie des periodischen Erbrechens mit Ketonaemie) H. Versé. Zeitschrift für Kinderheilkunde [Z. Kinderheilk.] 86, 1-30, 1961. 5 figs., bibliography.

The author has studied periodic ketonaemic vomiting in 190 children admitted to the Paediatric Clinic of the University of Cologne during the period 1949–59. He defines the condition as a specific metabolic reaction to emotional, allergic, infectious, toxic, traumatic, or dietetic stimuli, occurring as ketonaemic crises in constitutionally predisposed children. It is most commonly found in girls of the upper social classes living in towns, the average age of onset being 5½ years. Headache, malaise, irritability, apathy, and constipation may be present 1 or 2 days before the onset of the full-blown crisis, with continuous vomiting, at first of mucus and later of bile, with the odour of acetone in the breath and with ketonuria. The attack usually runs an afebrile course and terminates spontaneously in 24 to 48 hours.

The author underlines the gastro-intestinal, neurological, and psychological manifestations of ketonaemia. He found that in the intervals between crises radiological examination of the gastro-intestinal tract revealed no abnormalities. Within 1 or 2 hours of the occurrence of a crisis, however, there was almost complete retention of the contrast medium in the stomach. He considers that this disturbance of gastric motility is due to biochemical changes interfering with the vegetative innervation and that it may account for the frequent presence of abdominal colic. Among his patients the liver was enlarged in only 28 cases, jaundice was never encountered, and the results of liver function tests were almost always within normal limits. Ketonaemic crises are accompanied by primary and secondary manifestations in the central nervous system. Primary manifestations accompany the "early morning crises" and include syncope, clonic and tonic muscular cramps, lethargy or coma, and hyperpnoea. The child usually feels well within 24 hours. Secondary manifestations occur on the second or third day after the attack or even later and are due to loss of chlorides and fluids from vomiting. They include coma, tetany, neck rigidity, hyperpnoea, and diffuse abdominal pain with tympanites. Hypokalaemic or hypochloraemic alkalosis is frequently present, and its manifestations can be abolished by the administration of potassium chloride and glucose. The electroencephalograms of 6 children are described. Marked changes which occurred in them during ketonaemic crises disappeared completely in the intervals between crises.

Since emotional factors frequently provoke attacks of periodic vomiting and change of surroundings alone may prevent them, the author studied the psychological makeup of these children. He found that many were tense and highly strung and that a large proportion suffered from vegetative stigmata such as dermatographism. In 38% there was a history of domestic difficulties—for example, the mother went out to work, the parents were divorced, or the child was illegitimate, adopted, or a step-child. Nine cases are described in which psychological tests revealed a conflict situation in the life of the child. The value of such tests lies in the ability of the physician to discuss particular emotionally provocative situations with the parents and to suggest means by which they can be avoided, thus preventing the occurrence of periodic vomiting. E. S. Wyder

988. The Problem of Ketonaemia ("Acetonaemic Vomiting") in Childhood. II. Prognosis, Differential Diagnosis, and Clinical Judgment of Periodic Attacks with Ketonaemia. (Das Ketonamieproblem im Kindesalter ("acetonamisches Erbrechen") Klinische und experimentelle Untersuchungen. II. Zur Prognose, Differentialdiagnose und klinischen Beurteilung des periodischen Erbrechens mit Ketonamie)

H. Verse. Zeltschrift für Kinderheilkunde [Z. Kinderheilk.] 86, 137-169, 1961. Bibliography.

From his experience at the University Paediatric Clinic, Cologne, the author concludes that the prognosis of -periodic vomiting with ketonaemia in childhood is good, since the condition tends to disappear spontaneously with the onset of puberty, and deaths from it are relatively rare. Death may occasionally occur from circulatory collapse, either in a conscious patient during a vomiting attack, or in a patient who is comatose after an attack. The diagnosis is made (1) in the absence of an adequate anatomical cause for the vomiting; (2) on a history of at least 3 recurrent attacks; and (3) on proof that the accompanying ketonaemia or ketonuria is primary, all conditions in which they are secondary manifestations having been excluded. Assessment of the clinical picture is aided if it is remembered that statistical evidence demonstrates that the average age of onset of the disease is 5½ years, that it is more common in girls than in boys, in the upper than in the lower social groups, and in city than in country children, that a high proportion of these children suffer from vegetative stigmata, and lastly that a relatively large number of these patients come from unsatisfactory or broken homes.

In the differential diagnosis acute appendicitis and, to a lesser extent, other acute abdominal conditions must be borne in mind. Acetonaemic vomiting may be the first manifestation of diabetes mellitus before the onset of diabetic coma, while ketonaemia may be present in meningitis and in other diseases of the central nervous system. Periodic vomiting in neuropathic patients may or may not be accompanied by ketonaemia. Hypoglycaemia of organic origin rarely causes confusion, but functional hypoglycaemia may do so. The latter, however, occurs in the first 2 years of life and before the average age of onset of periodic vomiting with ketonaemia. In epidemic winter vomiting ketonaemia does not occur.

989. Liver Diseases and Osteoporosis in Children. I. Clinical Observations

CHING TSENG TENG, C. W. DAESCHNER JR., E. B. SINGLETON, H. S. ROSENBERG, V. W. COLE, L. L. HILL, and J. C. BRENNAN. *Journal of Pediatrics [J. Pediat.]* 59, 684–702, Nov., 1961. 16 figs., 30 refs.

The incidence of osteoporosis in chronic liver disease was studied in 26 children—7 with glycogen storage disease, 9 with primary hepatic tumour, and 10 with hepatic cirrhosis—most of whom were seen at the Children's and Jefferson Davis Hospitals, Houston, Texas. Osteoporosis was noted in 19 (6 with glucogen storage disease, 6 with primary tumour, and 7 with hepatic cirrhosis). In addition many suffered from muscle atrophy, retarded growth (10), loss of weight (7), and impairment of liver function (18). The case history of one child with a benign hepatoma is described to demonstrate the dramatic improvement which followed removal of the tumour.

The authors consider that these manifestations, especially osteoporosis, are all attributable to a systemic deficit of protein.

John Fry

990. Liver Diseases and Osteoporosis in Children. II. Etiological Considerations

CHING TSENG TENG, C. W. DAESCHNER JR., E. B. SINGLETON, and H. S. ROSENBERG. *Journal of Pediatrics [J. Pediat.]* 59, 703-709, Nov., 1961. 1 fig., 24 refs.

In this further paper on osteoporosis in liver disease [see Abstract 989] the authors discuss the various possible causes of the protein deficit which was considered to be responsible for the condition in 19 of the 26 children studied.

John Fry

991. Meckel's Diverticulum in Childhood

R. H. JACKSON and A. R. BIRD. British Medical Journal [Brit. med. J.] 2, 1399–1402, Nov. 25, 1961. 11 refs.

The authors report from the General Hospital, Newcastle upon Tyne, 82 cases of Meckel's diverticulum. These could be divided into three groups: (1) 28 in which there was intestinal obstruction; (2) 30 showing other symptoms; and (3) 24 which were asymptomatic. Of those in Group 1 the intestinal obstruction was due to bands or volvulus in 15 and to intussusception in 13. In Group 2 8 patients presented with an umbilical fistula or sinus, 17 with haemorrhage from peptic ulceration in

the diverticulum or adjacent jejunum, 4 with diverticulitis, and one with torsion. The 24 cases in Group 3 were found at laparotomy, performed for suspected intussusception or other reasons. There were 3 deaths in the series, 2 from intestinal obstruction and one from bronchopneumonia following reduction of an intussusception unassociated with the diverticulum. Thus the mortality in pathogenetic diverticula was only 2 out of 58 cases or 3.4%.

In cases presenting with obstruction the history was straightforward, namely, abdominal pain, copious vomiting, and constipation; the majority of these cases occurred in patients between 2 and 5 years of age. There were 8 cases of umbilical fistula or sinus; although only 180 cases of a complete fistula with faeces coming from the umbilicus due to a patent vitello-intestinal duct have been reported in the literature, 3 such cases occurred in this series. Of the 17 cases of peptic ulceration the ulcer perforated in '3 and the patient presented with peritonitis as well as haemorrhage; in 6 the intestinal haemorrhage was severe enough to warrant emergency operation, while in the remainder there was chronic bleeding and anaemia. The 4 cases of Meckel's diverticulitis were indistinguishable from appendicitis, and in one a foreign body was present. Of the 24 patients who were asymptomatic 10 were operated on for intussusception unassociated with the diverticulum. The authors do not consider, for statistical reasons given, that the presence of a Meckel's diverticulum predisposes to intussusception. Andrew Desmond

992. Primary Pulmonary Hypertension in Childhood J. F. FARRAR, R. D. K. REYE, and D. STUCKEY. British Heart Journal [Brit. Heart J.] 23, 605-615, Nov., 1961. 9 figs., 25 refs.

The authors describe 4 cases of primary pulmonary hypertension in children between the ages of 4 and 9 years seen at the Royal Alexandra Hospital for Children, Sydney, 3 of which (all fatal) were admitted within a period of 2 months; the condition was confirmed at necropsy. The patients presented with syncope of effort, cardiac pain, or dyspnoea, and in the 3 fatal cases death ensued within one year. The 4th child has maintained reasonable health over a period of 3 years. Drug therapy with anti-serotonin substances, steroids, anticoagulants, and reserpine was of no avail.

Examination showed palpable right ventricular overactivity and palpable pulsation of the pulmonary artery, an insignificant basal systolic murmur (with in one case a pulmonary diastolic murmur), an ejection click, and a very loud second pulmonary sound. In those with gross right ventricular dilatation the murmur of tricuspid incompetence was heard. Electrocardiography (ECG) showed right ventricular hypertrophy, and on exercise depression of the S-T segment, which was interpreted as evidence of cardiac ischaemia. Cardiac catheterization performed in all 4 cases revealed severe pulmonary hypertension without any evidence of a shunt. The heart was seen to be slightly enlarged in the radiographs, with a prominent pulmonary artery and proximal branches and very clear peripheral lung fields. Barium

injection of one necropsy specimen (illustrated) clearly revealed the tortuous proximal pulmonary arteries and deficient filling of the distal branches. Post mortem, right ventricular hypertrophy and some dilatation of the tricuspid valve were found. Recent thromboses were prominent throughout the pulmonary arteries, with unusual capillary formation around these in all 3 cases, while in the lungs musculo-elastic hypertrophy was present in arteries of all sizes down to capillaries; concentric intimal hyperplasia was rare. Histological examination of the pulmonary trunk showed an absence of the usual atrophy of elastic tissue, though this was not as dense or regular as that usually seen in the pulmonary arteries of the newborn.

In view of the acute course, the progressive ECG changes, and the changes in pressure the authors consider a congenital cause unlikely. They postulate as cause either a thrombosis secondary to peripheral venous emboli—though there was no macroscopic evidence of this—or an allergic arteritis.

H. G. Farquhar

993. Pyelonephritis in Infancy and Childhood J. B. Burke. Lancet [Lancet] 2, 1116-1120, Nov. 18, 1961. 14 refs.

The author reports the results of a follow-up study of 100 children who had been admitted to the Whittington Hespital, London, with pyelonephritis during the 10-year period 1950-60. The follow-up periods were 6 months to 1 year in 20 cases, 1 to 4 years in 52, 4 to 8 years in 23, and between 8 and 10 years in 5. When first seen 23 of the children were aged under 1 year, 19 were aged between 1 and 4 years, and 35 between 4 and 8 years, while 23 were over the age of 8. Since the series comprised 82 girls and 18 boys, females predominated in a ratio of 4.5:1; however, in the group under 1 year of age (16 girls and 7 boys) this predominance was less marked (2.3:1).

The data revealed that although routine inquiry had been made in the case of all the older children for details of abdominal pain and disturbances of micturition (frequency, dysuria, or enuresis), this was not invariably so in infants and younger children. It was also found that urinary infection was present in only one of 61 children. who had had one attack of pyelonephritis, in 4 of 18 who had 2 definite attacks, and in 3 of 11 children with a history of more than one attack, while of 10 children who had had recurrent attacks of pyelonephritis (3 ormore) 5 had either a urinary infection at follow-up or were being given prophylactic treatment. The importance of immediate examination of urinary cultures is stressed, since unless plating is carried out within an hour or so the growth of bacterial contaminants obscures the results. Pyelonephritis is usually a recurrent illness, and congenital abnormalities of the renal tract, if present, are a factor predisposing to recurrence. The present study showed no relationship between the likelihood of recurrence and the patient's age, length of follow-up, or duration of therapy. Second attacks occurred within one year of the first attack of pyelonephritis in 80% of the children who had recurrences, the symptoms being again similar to those observed in the first attack. Of

these 100 children followed up an abnormality of the renal tract was found in 6, and in one child necropsy revealed a large renal calculus. The author considers that a second attack of pyelonephritis, or a relapse during treatment, is an indication for radiological examination of the renal tract. But whether abnormalities of the renal tract are present or not, the appropriate use of drugs can often keep the urine free from infection and considerably ameliorate the symptoms, and so may prevent progressive pyelonephritic scarring. The authoremphasizes the necessity of follow-up studies in every child who has had pyelonephritis.

R. G. Meyer

994: Skeletal Changes in Infantile Hypothyroldism. (Sulle alterazioni scheletriche nell'ipotiroidismo infantile) G. Menichini and A. Ruiu. *Minerva pediatrica* [Minerva pediat. (Torino)] 13, 1601–1610, Nov. 24, 1961. 7 figs., bibliography.

The authors present a comprehensive review of the skeletal changes observed in hypothyroid infants and note that these are characterized by the discrepancy between the chronological age and bone age. The most persistent sign of hypothyroidism is the delay in the maturation of bones. They then describe 18 personal cases seen at the University Paediatric Clinic, Ferrara, in which serial radiographs were taken before, during, and after specific treatment of the hypothyroidism. They discuss both the changes in the epiphyses, which often show multiple foci of ossification (epiphysial dysgenesis), and the presence of a biconvex lens-shaped deformity of the dorsal and lumbar vertebrae, which they consider as a sign of severe pathological change before specific treatment is started. They conclude by stressing the value of repeated radiological examination, in view of the close correlation between the radiological changes and the degree of endocrine deficiency. Franz Helmann

995. The Acute Encephalopathies of Obscure Origin in Infants and Children

G. Lyon, P. R. Dodge, and R. D. Adams. *Brain* [*Brain*] **84**, 680-708, Dec., 1961. 9 figs., bibliography.

After reviewing the literature, the authors discuss the syndrome of acute encephalopathy in children on the basis of 16 cases seen at Massachusetts General Hospital, Boston, 7 of which they describe in detail. In all cases there was disturbance of consciousness from. drowsiness to coma, and all except 3 children had convulsions; no other neurological signs occurred regularly. There were no distinctive changes in the cerebrospinal fluid, although its pressure was raised in most cases. The condition was acute, with fever, nearly always arising from a non-specific febrile illness. In no case was there any evidence of a focal lesion in the cerebrum or brainstem. Many cases had some disturbance of salt and water metabolism, either from excessive administration or from excess loss. Difficulty in breathing was present in most cases owing to derangement of the respiratory mechanism or to dostruction of the airway; thus hypoxia was often an additional cause of the encephalopathy.

All but 3 of the 14 patients examined post mortem had swelling of the brain; 2 of the 3 were long-term

survivors and the other had hypertonic dehydration. No definite cellular or tissue changes could be found apart

from those due to hypoxia.

It is concluded that the condition described is an acute encephalopathy, closely related to febrile convulsions and febrile delirium. Death and permanent disability appear to be determined by hypoxia or ischaemia of brain tissue. The primary cause may be toxic. Suggestions are made for the management of the condition and the prevention of serious damage to the brain.

E. H. Johnson

996. Intellectual Impairment in Children with Localized Post-infantile Cerebral Lesions

J. McFie. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.] 24, 361-363, Nov., 1961. 27 refs.

At the National Hospital, Queen Square, London, 40 children, aged 5 to 15 years, who all had a unilateral pathological process in the cerebrum which had begun after one year of age and was later verified at fiecropsy or operation or by pneumoencephalography or the persistence of an electroencephalographic focus for at least one year, were subjected to the Terman-Merrill or Koh's blocks test or one of the Wechsler scales.

Differences in the I.Q. attributable to the site of the lesion in different groups of patients were not significant and no trend associating the I.Q. score with age at injury was found. In 15 cases, although a tendency for/verbal deficit to be associated with left-sided lesions and for performance deficit with right-sided lesions was observed; the association was not significant. No significant differences were found between left-sided and right-sided lesions for each Wechsler subtest, although the direction of differences was similar to that of adults in the digitspan, similarities, picture-arrangement, and blockdesign tests. In 26 cases, differences between the mean scores of the "memory for designs" test in patients with left- and right-sided lesions were highly significant, and a significant association was also found between site of the lesion and the extent of test-deficit. In these children, as in adults, there was no difference between patterns of impairment in the right-handed patients and the 4 lefthanded patients in the series.

It is postulated that within the age range of the children tested on the picture completion subtest (9 to 15 years) the cerebral organization mediating the function has become established in adult form. Differences from the pattern of deficit normally found in adults were shown in the vocabulary test and the digit symbol test.

G. de M. Rudolf

997. Disturbances of Manual Perception in Children with Cerebral Palsy

C. Monfraix, G. Tardieu, and C. Tardieu. Cerebral Palsy Bulletin [Cerebral Palsy Bull.] 3, 544-552, Dec., 1961. 6 figs.

The recognition of shapes held in the hand without the help of sight is one of the gnosias that should be studied in children with cerebral palsy. We have compared, in identical conditions, the responses given by 218 normal children with those given by 92 children with cerebral palsy. It is possible to establish the existence of disorders of manual perception, and to judge the severity of this type of agnosia, by comparing a child's gnosic age and mental age. This procedure provides a useful check on progress during re-education.

The present study shows that disorders of manual perception can be found in all-forms of cerebral palsy. This type of agnosia occurs more frequently, and is often more severe, in cases with spasticity or rigidity than in those with athetosis. It is perhaps more frequent in cases where the right side is affected rather than the left, and possibly also in unilateral rather than bilateral cases.—[Authors' summary.]

998. Development of Manual Perception in the Child with Cerebral Palsy during Re-education

C. MONFRAIX and G. TARDIEU. Cerebral Palsy Bulletin [Cerebral Palsy Bull.] 3, 553-558, Dec., 1961. 4 figs.

In every case of cerebral palsy it is essential to examine the gnosias: recognition of objects field in the hand, recognition of the position occupied by the parts of a limb in space, tactile discrimination, body image, and the "extinction phenomenon". In the present study we have reported only on the progress made during re-education in the ability to recognize shapes held in the hand.

When we speak of the gnosic quotient we mean the relation between the gnosic age (established by comparison with the responses of children of the same mental age) and the mental age. Even when the gnosic disorders are profound (gnosic quotient less than 50), re-education can result in a considerable improvement, or in the disappearance of the disorders. This reducation has to be very prolonged and must not be interrupted. Fallings off are frequent when re-education is interrupted.

It seems permissible to contrast agnosias caused by a lesion, in which re-education produces only long-term success, with agnosias caused by lack of use, in which results are much more quickly obtained.—[Authors' summary.]

999. The Child Who Refuses to Attend School T. P. MILLAR. American Journal of Psychiatry [Amer. J. Rsychiat.] 118, 398-404, Nov., 1961. 16 refs.

School phobia is now a well recognized entity in Britain. and many local authorities have emphasized the need for urgent action when a child who has this phobia comes to the notice of a paediatrician. The present author first discusses the subject in broad outline and then describes. what he terms the "acute school refusal". This would appear to be a manifestation of a disturbance in the mother-child relationship, in which the mother is overindulgent with the child stemming from her own personal problems. The childhood neurosis revealing itself as school phobia involves a disturbance of affect, behaviour, and self concept. The author outlines the methods and principles of dealing with the condition by urgent psychotherapy for the child and psychiatric case work with the parents as well as by insisting on immediate return to school; he contends that with this treatment the prognosis is good. David Morris

Medical Genetics

1000. Risk of Parents Who Have Had One Child with Down's Syndrome (Mongolism) Having Another Child Similarly Affected

C. O. CARTER and K. A. EVANS. Lancet [Lancet] 2, 785-788, Oct. 7, 1961. 11 refs.

Between 1944 and 1955, 725 patients (index cases) with mongolism (Down's syndrome) domiciled in or near London were seen at the Hospital for Sick Children, Great Ormond Street, London, and of these, 642 have been followed up and family data collected. To these families 927 sibs were born before the index patient and among these were 4 mongols, while of 312 sibs born after the index patient 5 were mongols. The corresponding numbers of mongols expected on the basis of the prevalence of mongolism in the general population are ,1.5 and 1. In these families neither the stillbirth rate nor the miscarriage rate differed significantly from that in the general population. The ratio of the number of mongol sibs found to the number expected was clearly related to the age of the mothers at the birth of the index patient.

It appeared from this study that the risk of a second mongol being born is some 50 times the random risk when the mother is under 25 years of age, 5 times the random risk for mothers aged 25 to 34 years, and not increased for mothers aged 35 years or over. In 3 of the 4 instances in which a mother bore a mongol child before the age of 25 and then had a second affected child, it was shown by Hamerton et al. [see Abstract 1001] that one or other parent had a chromosome abnormality. The authors therefore conclude that for younger mothers chromosome studies are desirable before genetic counsel is offered. It is suggested that parents who have had one mongol child may be told that, provided they have no other close relative similarly affected, the risk of having a second mongol child is of the order of 1 to 2%, irrespective of maternal age.

[The reasons for considering the index cases with younger and older affected sibs separately are not clear.]

A. G. Baikie

1001: Chromosome Studies in Detection of Parents with High Risk of Second Child with Down's Syndrome J. L. Hamerton, S. M. Briggs, F. Giannelli, and C. O. Carter. Lancet [Lancet] 2, 788-791, Oct. 7, 1961. 5 figs., 6 refs.

These studies were carried out at Guy's Hospital and the Institute of Child Health, London, as a second stage in the investigations reported by Carter and Evans [see Abstract 1000]. Chromosome studies were restricted to the index patients with a mongol sib, the affected sib, their parents, and in some families the grandparents. Of 5 families with an index patient and an affected younger sib, 3 were found to have translocations or isochromosomes involving chromosome No. 21. In one

family the child, its mother, and the mother's mother allcarried a 15/21 translocation (Carter et al., Lancet, 1960, 2, 678; Abstr. Wld Med., 1961, 29, 337). In anotherfamily both mongol children had died, but the mother was found to have a 21/21 or 21/22 chromosome translocation. In yet another family the mongol child and his father were both found to be mosaics and both seemed to carry an isochromosome for the long arms of chromosome No. 21. The father probably had a majority of normal male cells and a minority of cells which were effectively trisomic for chromosome 21. Of the mongol child's two cell lines, one was effectively trisomic and the other effectively tetrasomic for chromosome 21. In the remaining 2 families in which there were younger affected sibs, the parents were of normal karyotype and the mongols were of the common 47-chromosome type. The findings were the same in the 4 families with an index: patient and an older affected sib.

In discussion it is pointed out that in 4 of the 9 families in the series having 2 affected sibs, both mongols were born before the mother had reached the age of 30. In 3 of these 4 families a chromosome abnormality was found in one or other parent. [It is fair to point out that in 4 other families without demonstrable chromosome abnormality the first affected sib was born before the mother reached the age of 30.] The possibility is accepted that there is an increased risk of a second child being affected when a young mother bears a common 47-chromosome mongol and neither parent has an obvious chromosome abnormality. This may be due to an inherited predisposition to non-disjunction or to the occurrence of "trisomy 21/normal" mosaicism in one or other parent. The demonstration that a first mongol is not of the common 47-chromosome type, or that one parent has a chromosome abnormality, points to an increased risk of a second child being affected. Even where the affected child is a normal trisomy-21 mongol and neither parent has a demonstrable chromosome abnormality the risk is nevertheless increased and the degree of increased risk may be related to the mother's A. G. Balkie age.

1002. Pericentric Inversion of Chromosome 21: a Possible Further Cytogenic Mechanism in Mongolism J. E. Gray, D. E. Mutton, and D. W. Ashby. Lancet [Lancet] 1, 21-23, Jan. 6, 1962. 8 figs., 5 refs.

1003. Triple Mosaicism of the Sex Chromosomes in Turner's Syndrome and Hirschsprung's Disease
M. D. HAYWARD and A. H. CAMERON. Lancet [Lancet] .
2, 623-627, Sept. 16, 1961. 7 figs., 22 refs.

At the Children's Hospital and the University Department of Genetics, Birmingham, the examination of buccal mucosal smears in 2 female children showed an abnormal sex-chromatin pattern. Because of this find-

ing chromosome studies were undertaken and both were found to be cases of triple mosaicism of sex chromosome constitution XO/XX/XXX. The first patient, aged 10 years, was a mentally subnormal child of short stature with abnormal metacarpals and syndactyly of the middle 3 toes of both feet. The second case was in a female infant aged 3 days with Hirschsprung's disease, in whom an unusually long segment of narrowed bowel was found. In the first case 11% of the buccal mucosal cells contained sex chromatin and 12% of the positive cells had double chromatin bodies, while in the second 5 to 9% of the cells were positive, but no double chromatin bodies were found.

The genesis of such mosaics is discussed and it is pointed out that in both the present cases mosaicism must have arisen at or after the second cleavage division of the zygote. The relationship between the XO state and the clinical picture of Turner's syndrome is considered. It is suggested that the clinical picture is unlikely to be due simply to loss of an X chromosome. The authors also discuss the possible relationship in their second case between sex chromosome abnormality and Hirschsprung's disease. They report similar studies in 2 other female children with the latter disease, both of whom were normally chromatin-positive and of XX sex chromosome constitution.

1004. Deletion of Y Chromosome in a Family with Muscular Dystrophy and Hypospadias

S. MUIDAL and C. H. OCKEY British Medical Journal. [Brit: med. J.] 1, 291-294, Feb. 3, 1962. 6 figs., 13 refs.

1005. Differential Transmission of Down's Syndrome (Mongolism) through Male and Female Translocation Carriers

J. L. HAMERTON, V. A. COWIE, F. GIANNELLI, S. M. BRIGGS, and P. E. POLANI. Lancet [Lancet] 2, 956-958, Oct. 28, 1961. 3 figs., 13 refs.

The authors report from the Maudsley and Guy's Hospitals, London, an extensive family in which the index patient had 46 chromosomes and translocation of chromosomes 15/21 resulting in Down's syndrome (mongolism), and in which 14 clinically normal carriers with 45 chromosomes and 15/21 translocation were found. Examination of a biopsy specimen from one of the male translocation carriers in the family showed that in most cells in diakinesis 22 bodies were seen, 21 bivalent and one trivalent. This confirms the hypothesis that the abnormal chromosome seen was in fact produced by translocation.

In this family, and in others reported with mongolism associated with 15/21 chromosome translocation, the translocation has always come to the affected child from the mother. A table shows that the 28 living offspring of the 8 known maternal carriers include 12 patients with mongolism, 15 clinically normal carriers, and one chromosomally normal child. The 11 living offspring of the 2 known carrier fathers comprise no patient with mongolism, 11 carriers, and no normal children. These findings can best be explained by preferential segregation of the chromosomes in the trivalent and selective fertiliza-

tion. It is suggested that the sperm carrying only the 15/21-chromosome has a selective advantage over the sperm carrying a normal complement of chromosomes, and that in the female the meiotic system favours recovery of the translocation chromosome.

C.O. Carter

1006. Heredity in Common Diseases: a Retrospective Survey of Twins in a Hospital Population

A. G. MARSHALL, E. O. HUTCHINSON, and J. HONISETT. British Medical Journal [Brit. med. J.] 1, 1-6, Jan. 6, 1962. 1 fig., 33 refs.

A total of 2,537 pairs of twins have been discovered among hospital patients: 1.725 pairs were found in the hospitals of the Wolverhampton Group and 812 pairs in the General Hospital, Birmingham. The twins were divided into identical and fraternal pairs by personal inspection and questioning and by family opinion. The sex ratios and the proportions of identical and fraternalpairs were compared with a previous collection of twins from the same district. Analysis of these factors confirms that this series is reasonably free from bias. There is some evidence to suggest that the previously reported increased mortality of males compared with females is less marked than before. Retrospective medical histories were taken individually from the whole collection: After scrutiny and checking these histories were classified: and the results analysed.

The incidence of 24 common diseases in this series was examined by the method of concordance and dis- > cordance. In 8 such diseases the numbers were insuffici-, ent for analysis. In 12 diseases there is evidence of a hereditary factor; the strength of this evidence varies: They are appendicitis, benign growth, chest infections, otitis media, eczematous dermatitis, epilepsy, hernia, infective hepatitis, rheumatism, sinusitis, squint, and varicose veins. In all but one of them there are already records to suggest an inherited trait. The exception is infective hepatitis. While our evidence is somewhat tenuous it is suggestive of a genetic factor in susceptibility to this disease. In the remaining 4 conditions our results suggest that there is no genetic background, and they are in accordance with previously published work except in one instance. The exception is pulmonary tuberculosis. Comment is made on its different background from recurrent chest infections, in which our results show clearly that there is an inherited factor, and on the fact that our findings differ from those of previous investigators.

From our experience in making this survey we support Burnet's suggestion [Lancet, 1953, 1, 104] for the establishment of permanent twin research departments in certain centres.—[Authors' summary.]

1007. A Case of XXXXY Klinefelter's Syndrome J. H. Fraser, E. Boyd, B. Lennox, and W. M. Dennison. Lancet [Lancet] 2, 1064–1067, Nov. 11, 1961. 5 figs., 15 refs.

1008. Applications of Genetics in Psychlatry and Neurology.

L. A. Hurst. - Eugenics Quarterly [Eugen. Quart.]-8, 61-80, June [received Oct.], 1961. 47 refs.

Public Health and Industrial Medicine

1009. Absenteeism among School Children and Water Fluoridation

G. WYNNE-GRIFFITH. Medical Officer [Med. Offr] 106, 393-395, Dec. 29, 1961. 3 refs.

Fluoridation of the water supply in Anglesey began in November, 1955—that is, during the school year 1955-6. The study described in this paper was designed to determine whether the introduction of fluoridation had any adverse effect on school attendance, and for this purpose the records of absenteeism among 4,750 children, aged 5 to 11 years, who attended school in the 10-year period 1951-60 were analysed. A total of 54 schools were divided into 3 groups according to the fluoride status of the water used for domestic purposes by the population which each school served—a fluoride content of 0.1 p.p.m. 22 schools, 0.7 p.p.m. 10 schools, and 1.0 p.p.m. 22 schools. Attendance in all 3 groups of schools improved after 1955, the improvement being greater (though not significantly so) in the last group. It is pointed out that fluoridation has no beneficial effect (except on the teeth) and a marked improvement in the dental health of children of school age could not be expected so soon after the introduction of fluoridation. The findings do confirm, however, that the increase in the amount of fluoride in the water supply had no adverse effect on health and was not followed by any specific illness; moreover, water with the high fluoride content did not increase liability to other illnesses or alter the normal course of recovery from them. J. Cauchi

1010. Brucellosis—an Island Epidemiological Study M. Brodigan, A. McDiármid, P. G. Mann, and J. F. Skone. British Medical Journal [Brit. med. J.] 2, 1393–1396, Nov. 25, 1961. 18 refs.

An interesting epidemiological study of the incidence of brucellosis in cattle and in man was carried out in the Isle of Wight. Out of 19 patients with suspected active infection, in 4 a positive diagnosis was made on the basis of history, clinical condition, brucellin skin tests, and agglutination titres before and after treatment with a combination of streptomycin and tetracycline; the therapeutic response was satisfactory. Surveys of persons thought to be occupationally exposed to infection or known to consume raw infected milk showed the highest rate of positive skin reactions and of agglutination titres over 1:20 in veterinary surgeons (7 out of 8), and the next highest rates among abattoir workers and persons taking infected milk; on this basis it was estimated that about 17% of the adult population were infected, the great majority of infections being inapparent. The incidence of positive skin reactions was also high (17%) 'among a group of 85 children who attended rural schools and drank raw milk at home.

On the basis of tests on 2,480 churn samples of milk 6.3% of dairy herds on the island were found to be

infected, and individual samples from 338 cows in 20 different herds showed that about 10% were positive by the milk inoculation test in guinea-pigs. *Brucella* infection is thus widespread among the dairy herds in the island, from which it is transmitted to man.

H. Stanley Banks

1011. An Analysis of Tetanus Prophylaxis in 3,455 Cases P. M. Binns. British Journal of Preventive and Social Medicine [Brit. J. prev. soc. Med.] 15, 180–185, Oct., 1961.

Between June, 1958, and March, 1959, a total of 3,455 patients attending the Public Dispensary, Leeds, received tetanus prophylaxis for wounds which were more than 3 hours old, already infected or contaminated with soil or manure, deep and penetrating, with devitalized tissues, or incompletely closed. To a patient with a history suggesting immunization with tetanus toxoid since 1939 a booster dose of the toxoid was given; in other cases 0.9 ml. of tetanus antitoxin was given intramuscularly half an hour after a trial dose of 0.1 ml. subcutaneously. Of the 3,455 patients 2,726 (79%) received antitoxin in full standard dosage of 3,000 units and 729 (21%) received the toxoid. The percentage incidence and times of onset of local and general reactions to the serum are tabulated and analysed.

In the discussion it is noted that subjects who have been actively immunized against tetanus retain a measurable level of tetanus antitoxin in the serum for at least 11 years and respond actively within a few days to a booster injection of toxoid. The only section of the population with such basal immunity are ex-Servicemen, and the majority of these require booster injections to retain this immunity, which would call for "an effort on a national scale". In boys, mortality from tetanus is highest in the age group 5 to 14 years; since this age group is almost entirely without active immunization the need for routine immunization against tetanus in infants or young children is apparent.

The incidence of local reactions to serum was higher in subjects who had had previous antitetanus serum than in those who had not, while the incidence of both local and general reactions was higher in those who had had asthma or infantile eczema than in those without these predisposing factors. In the author's view such subjects. and preferably all those giving local reactions, should be followed up and actively immunized against tetanus. It is suggested that in the present series the administration of antihistamines to subjects giving a local reaction may have prevented the development of more serious reactions. The author considers, contrary to the views of Laurent and Parish (Brit. med. J., 1952, 1, 1294), that local reactions are important. But the majority of the "local reactions" in the present series were delayed, occurring 6 to 10 days after the injection and in some instances 8 to 24 hours or less before the general reaction. These might more properly be considered to be local

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'manifestations of the general reaction, and do not, in the abstracter's view, invalidate the test for serum sensitivity of Laurent and Parish.]

H: Stanley Banks

1012. Live Pollomyelitis Virus Vaccines. - Present Status and Problems for the Future

-H. KOPROWSKI. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 1151-1155, Dec. 23, 1961. 3 figs., 9 refs.

INDUSTRIAL MEDICINE

1013. Some Aspects of Fatigue among Air Crews Employed in Commercial Aviation. (Quelques aspects de la fatigue dans l'aviation de Transport)

P. BUGARD and M. HENRY. Presse médicale [Presse méd.] 69, 1903-1906, Oct. 21, 1961. 6 figs., 38 refs.

Since the beginning of air travel, fatigue affecting air crews has posed many problems in relation to the efficiency of members of the crew and consequently to the safety of passengers. The introduction of large jet aircraft flying at high altitudes and at very high speed has aggravated these problems, particularly as on long intercontinental flights persons may be transported within a few hours from one extreme of climate to another. Also the environmental conditions within the pilot's cabin of jet planes may approximate to tropical conditions. All these factors influence the physical and emótional condition of the crews, particularly the captain, who carries the main burden of responsibility. The general aspects of the subject were examined by the authors in a previous paper (Presse med., 1961, 69, 1104). In the present paper they present their findings on three specific items. based on investigations carried out on the crews of 13 intercontinental commercial aircraft (of which 11 were jet planes) in whom measurements were made of the urinary content of aldosterone, 17-ketosteroids., 17hydroxycorticoids, and creatinine. The results are tabulated. Concomitantly, disturbance of neuromuscular activity was confirmed by electric stimulation tests on . the skin and nerves. In each case the captain of the aircraft appeared to be more severely affected than other members of the crew.

The authors suggest that these measurements reflecting endocrine and metabolic changes might be applied to the detection of fatigue in flying personnel.

[This well documented article is commended to the notice of all interested in aviation medicine. A useful bibliography is appended under the separate headings: aldosterone, 17-ketosteroids and corticoids, and neuro-muscular excitability.]

• A. Meiklejohn

1014. Permanent and Temporary Diesel Engine Noise Dips

D. W. Gravendeel and R. Plomp. Archives of Otolaryngology [Arch. Otolaryng.] 74, 405-407, Oct., 1961. 3 figs., 1 ref.

In an earlier study the authors investigated the question of whether the temporary and permanent "dips" in the audiogram caused by the same noise showed any degree

of resemblance, since the answer would help to decide whether data from temporary-noise deafness apply to the causation of the irreversible dip. They concluded then that there is no simple relation between hearing loss immediately after the firing of fire-arms and the ultimate permanent loss and suggested that this may be because either temporary and permanent loss has each its own genesis or alternatively that permanent loss arises from temporary loss by incomplete and asymmetrical recovery.

In the present study they investigated the hearing loss resulting from continuous noise, in this case that of. diesel engines. Of 48 subjects aged from 31 to 51 years who had been exposed to diesel engine noise for 1 to 10 years, 32 showed "dips" in the audiogram from one or both ears of 30+ decibels, mostly at 5.4 kc.p.s., and this was independent of age or extent of loss. The octave-band of the noise showed an average of 100 db. with maximum frequency at 2,000 c.p.s. From this study they conclude that, for continuous noise at any rate, the two dips, that is the reversible and the irreversible, are "possibly" brought about by the same mechanism, and the permanent hearing loss follows from the temporary loss by incomplete and asymmetrical recovery. Thence, for continuous noise, it is justifiable to consider data from experiments on temporary noise deafness, as applicable to the problem of irreversible noise dips.

[A useful paper, but it throws no light on the problem of individual sensitivity to noise-damage.]

F. W. Watkýn-Thomas

1015. Damage Risk Criteria and Noise-induced Hearing Loss

A. GLORIG, W. D. WARD, and J. NIXON. Archives of Otolaryngology [Arch. Otolaryng.] 74, 413-423, Oct., 1961. 16 figs., 3 refs.

In this attempt to establish some means of estimating the liability to noise induced deafness the investigation was limited to the effect of continuous noise, which is defined as noise having no noticeable sharp peaks or changes in level, as opposed to "impulse noise", in which the level changes suddenly. In the authors' words: "Limited laboratory research indicates that the laws governing T.T.S. (temporary threshold shifts) from exposure to steady noise (non-impulse) do not operate for impulsive noise exposure since the response of the basilar membrane to steady noise and to impulse noise should be completely different. For the present, we can only say that no one should be habitually exposed to impulse noise of any considerable magnitude without the use of hearing conservation measures:"

It is concluded as a result of the authors' various studies that (1) if there is no T.T.S. there will be no P.T.S. (permanent threshold shift); (2) if the resting threshold is elevated the magnitude of the T.T.S. will be proportionately less; (3) a specific noise exposure (level and time combined) will produce a corresponding specific T.T.S.; (4) a specific exposure (level and time combination) will produce a specific amount of P.T.S.; and (5) the progression of P.T.S. is similar to that of T.T.S., but on a different time scale. Study of T.T.S. indicates

that continuous steady noise with a sound pressure level of less than 80 decibels (approximately 78 db.) will not produce significant T.T.S. The maximum change due to exposure occurs within 10 to 12 years, regardless of exposure level. After 10 years the level shifts, but the shift parallels the shift indicated for age effect. Each different noise level, provided time is constant, produces a specific shift. The authors suggest that from the use of formulae developed from study of the temporary shifts (and described in this paper) it should be possible to predict the ensuing permanent shift. They also suggest "hearing conservation criteria" for noise exposure "as a function of the relation between time and sound pressure level".

F. W. Watkyn-Thomas

1016. Myocardial Damage in Caisson Workers. (Die Myokardschädigung der Caissonarbeiter)

I. RÓZSAHEGYI and I. KENEDI. Archiv für Gewerbepathologie und Gewerbehygiene [Arch. Gewerbepath. Gewerbehyg.] 18, 610-631, 1961. 3 figs., 14 refs.

Working at the State Institute of Industrial Medicine. Budapest, the authors have sought to ascertain: (1) whether electrocardiographic (ECG) changes are more frequent in caisson workers than in others doing work of equal severity but not exposed to compressed air; (2) what such ECG changes are; and (3) how the changes observed are associated with working in compressed air. Accordingly they recorded 459 ECG tracings from 316 persons employed on caisson work in the construction of the Budapest underground railway, 2 or more tracings being obtained in 85 cases at various intervals. These records, which were by no means uniform, were then compared with those from 100 persons of corresponding ages doing equally hard work. In all, 308 tracings from caisson workers were compared with 300 from the controls, all of whom showed some ECG change. The proportion of ECGs showing changes in the three age groups 20 to 29, 30 to 39, and 40 to 49 years were, for caisson workers, 25, 25, and 37%, with a mean for all ages of 28%; for the control group the corresponding figures were 11, 15, and 13%, with a mean of 13% for all ages. The differences for age group 40 to 49 and for "all ages" were statistically significant (P<0.1). The ECG changes included high P2 and P3 waves (P pulmonale), prolonged P-Q, a widened QRS complex, S-T flattened even to below the isoelectric point, flat T₁ (and/or T2) wave, and irregular sinus arrhythmia (but the number of cases with the last named sign and of those with a wide QRS were too small to permit of any conclusions being drawn). The high P wave (P pulmonale) was the most frequent finding and appears to be the typical sign of overload on the right heart. It can occur without any of the signs of decompression trauma. In the 20 to 29 age group it was most frequent in the first year at such work, but high P waves were significantly more frequent in the older age groups, suggesting that caisson work potentiates changes due to ageing; it was also definitely associated with the length of time at such work. Low S-T was not common and was not associated with ageing or with duration of exposure, but was definitely associated with the number of attacks of caisson

disease. In some cases it appeared to be a manifestation of myocardial fibrosis.

It was found that some of the ECG changes were reversible and diminished gradually if the patient was removed from caisson work. It is suggested that the changes seen may be due to air embolism of twigs of the pulmonary or even the coronary arteries, but in view of the relatively short follow-up period (4 years) it is still not certain which changes are permanent and which are temporary. As a control measure the value of recording the ECG before men start caisson work, and again at regular intervals during such employment is emphasized. Finally the clinical histories of 3 patients are presented. All 3 had had attacks of caisson disease and in 2 there was considerable involvement of the central nervous system even 4 years after the last attack, while ECG changes were still present:

[Apparently none of the patients had worked at more than 1.8 atmosphere and 50 of the total number had had more than 6 attacks of caisson disease, but within what period of time is not stated.]

W. K. Dunscombe

1017. Observations on the Late Effects of Internally Deposited Mixtures of Mesothorium and Radium in Twelve Dial Painters

W. H. BAKER, J. B. BULKLEY, R. A. DUDLEY, R. D. EVANS, H. B. McCLUSKEY, J. D. REEVES JR., R. H. RYDER, L. P. SALTER, and M. M. SHANAHAN. New England Journal of Medicine [New Engl. J. Med.] 265, 1023-1028, Nov. 23, 1961. 2 figs., 5 refs.

The authors report the results in 12 women who had been employed as luminous-dial painters mainly in the early 1920's and were later investigated clinically and by radiation dosimetry during the years 1952-60 at the Massachusetts General Hospital, Boston. The mixture forming the luminous paint contained both radium and its isotope mesothorium, small quantities of which were ingested as it was the habit to bring the brushes used in the work to a fine point with the lips. The internal radiation resulting from the deposition of the two radioactive substances, primarily in the skeleton, was therefore estimated. Since rather over half the radon (to which radium decays by alpha-ray emission) is exhaled, its activity was measured by alpha-ray counts on the breath. The rest of the radon, which remains in the body, decays into other isotopes with emission of alpha, beta, and gamma rays, and its activity was measured by counts of the gamma rays emitted, the detector being placed in most cases at the base of the spine. For mesothorium the latter method could be used successfully in only 3 of the subjects, on account of the relatively short half-life (5.7 years) of this isotope; and the thoron to which it decays, having an extremely short half-life (52 seconds), could of course not be determined by exhalation measurements. In 2 of the 12 subjects the mesothorium values were obtained by analysis of the amount of mesothorium and radium in samples of bone or teeth.

From these direct measurements initial mesothorium: radium activity ratios for the representative year 1924 were obtained for 5 subjects; in the remaining 7, in

whom current activity from mesothorium deposition could not be directly estimated, the ratio was taken as 6.0, this being the average figure obtained from a total of 15 persons who had worked at the same establishment at about the same time. The results indicated that, with one exception, approximately 90% of the skeletal irradiation was attributable to the mesothorium. The relevant clinical occurrences were fractures, presumably pathological, in 7 subjects, including 2 cases of multiple fractures; carcinoma of the nasal sinus in one case; x-ray evidence of radiation osteitis of long bones and skull in all cases: and dental caries or pyorrhoea at some time in all subjects, but with x-ray evidence of radiation osteitis of the jaw in one only. There was a correlation between the severity of the clinical changes and the amount of radioactive material retained. There were no instances of any blood dyscrasia due to radiation.

J. J. Segall

1018. Human Orf: Isolation of the Virus by Tissue Culture

J. NAGINGTON and C. H. WHITTLE. British Medical Journal [Brit. med. J.] 2, 1324–1327, Nov. 18, 1961. 6 figs., 19 refs.

1019. Byssinosis in Flax Workers

A. BOUHUYS, J. VAN DUYN, and H. J. VAN LENNEP. Archives of Environmental Health [Arch. environm. Hlth] 3, 499-509, Nov., 1961. 2 figs., 22 refs.

The authors, who report from University Hospital, Leiden, have studied a group of 39 workers exposed to the dust of flax in a large factory in the Netherlands where 9,000 tons of cropped flax are processed yearly. The cropped flax is first de-seeded mechanically and then retted. In this process the fibres are loosened from the woody parts of the plant by a putrefactive process carried out in the open air in concrete containers filled with water, which takes 5 or 6 days. The retted flax is subsequently dried, after which it is subjected to further processing.

It was found that of 24 workers who were exposed to the dust of the retted flax 16 (67%) showed some evidence of byssinosis. A small but significant decrease in F.E.V.0.75 was observed on Monday after a free weekend in workers handling the retted flax, but no change in this volume was found 2 days later. The workers with byssinosis had slightly lower starting values on Wednesday than on Monday, a difference which was probably significant. The workers on the retted flax also showed a leucocytosis developing on Monday and also during the course of every working day.

It is regarded as matter for speculation whether the substance which induces the leucocytosis is identical with that responsible for the dyspnoea. It is suggested that the substance or substances are contained in the dust of dried retted flax and probably originate as the products of metabolism of bacteria or fungi, or both, during the process of flax retting. Workers exposed to the dust of retted flax for more than 10 years have significantly decreased ventilatory capacity and other changes of respiratory function similar to those found in obstructive emphysema; it is therefore thought that

exposure to the dust of retted flax causes an impairment of respiratory function and permanent lung damage.

Kenneth M. A. Perry

INDUSTRIAL TOXICOLOGY

1020. The Detection of Lead Retention by Means of a Lead Mobilization Test. (Le dépistage de l'imprégnation saturnine par un test de mobilisation du plomb)
C. ALBAHARY, R. TRUHAUT, C. BOUDENE, and H. DESOILLE. Presse médicale [Presse méd.] 69, 2121-2123, Nov. 11, 1961. 28 refs.

A method for detecting minimal degrees of lead retention resulting from occupational exposure by measuring the mobilization and excretion of lead produced by the chelating agent sodium calciumedetate is described in this paper from the Institute of Industrial Hygiene and the Hôpital Saint-Denis, Paris. The urinary lead content is first estimated on a 24-hour specimen of urine. On the following day, having emptied the bladder, the subject drinks 300 ml. of water to promote a diuresis. Sodium calciumedetate, 0.5 or 1.0 g., is then injected intramuscularly or given diluted in isotonic glucose by intravenous drip, the results being similar with both quantities and both routes of administration. Maximum lead excretion takes place within 5 hours, and the lead concentrations in the urine at either 5 or 10 hours as well as in the whole 24 hours following administration of the chelating agent are estimated.

In 20 normal subjects the 24-hour urinary excretion of lead rose from between 10 and 85 µg, to between 85 and 465 μ g. For the same period lead excretion rose from 55 to 300 μ g. to 1,200 to 8,105 μ g. in 11 patients with mild chronic lead poisoning, from 110 to 520 µg, to 940 to 6,975 µg. in 12 symptomless subjects exposed occupationally to lead, and from 40 to 100 μ g. to 450 to 920 μ g. in 9 out of 16 subjects possibly exposed to lead but not otherwise than by this test showing any evidence of exposure. (The excretion levels at 5 and 10 hours after administration of the chelate are also reported.) The authors suggest that a level of 700 μ g. per litre for the 24 hours following the injection, and 800 µg, per litre for the first 5 or 10 hours, indicate abnormal lead retention. It is concluded that this is a specific test for lead retention, the use of which is indicated when the urinary lead excretion is normal (upper limit, 80 µg. in 24 hours), but principally for the detection of slight absorption from lead dust or vapour. It is stressed that such slight retention of lead should not be neglected, since there is always a possibility that it may cause renal damage.

J. J. Segall !

1021. A Rapid Method for the Micro-estimation of Lead in Urine

J. M. DICK, R. W. ELIJS, and J. STEEL. British Journal of Industrial Medicine [Brit. J. industr. Med.] 18, 283–286, Oct., 1961. 2 figs., 2 refs.

A method is described for the determination of microgram quantities of lead in small volumes of urine. Recoveries from urine samples of added lead show that the mean results of triplicate analyses will, 19 times out

of 20, lie within $\pm 12.5 \,\mu g$, per litre of the true concenof urine may be carried out in three hours.—[Authors' summary.]

1022. Human Exposure to Carbon Tetrachloride Vapor: Relationship of Expired Air Concentration to Exposure and Toxicity.

R. D. STEWART, H. H. GAY, D. S. ERLEY, C. L. HAKE, and J. E. Peterson. Journal of Occupational Medicine [J. occup. Med.] 3, 586-590, Dec., 1961. 1 fig., 9 refs.

From the Medical Department and laboratories of the Dow Chemical Company, Midland, Michigan, the authors describe 3 series of experiments in which the concentration of carbon tetrachloride (CCl4) in the expired air of human subjects was measured by infra-red spectrometry after their exposure to various concentrations of CCla vapour. The concentrations of CCla in the blood and urine were measured concurrently, but were not detectable by infra-red analysis. The subjects were healthy males aged 30 to 54 years. In order to simulate brief over-exposure 6 men were exposed to a concentration of CCl₄ vapour of 49 p.p.m. for 70 minutes. In addition, 6 subjects were exposed to 11 p.p.m. for 180 minutes and again later to 10 p.p.m. for 180 minutes. Several subjects took part in all 3 experiments, which took place at 4-week intervals. Before, during, and after each exposure samples of blood, urine, and expired air were analysed for CCL. The serum glutamicoxalacetic transaminase activity and urinary urobilinogen content were also measured before and at intervals after exposure. In some subjects in the first experiment, the serum iron concentration and 15-minute phenolsulphonphthalein excretion were determined and the urine analysed before and after exposure. Samples of expired air were collected in 6-litre Saren bags. (These may be sealed and sent to a distant laboratory for analysis.) The air was then scanned by an infra-red spectrometer after being drawn into an evacuated gas cell.

- No changes were noted in serum transaminase activity, phenolsulphonphthalein excretion, or urinary content of blood and albumin, but in the group exposed to 49 p.p.m. of CCl₄ for 70 minutes the serum-iron level of 2 of the 4 subjects studied showed falls of 40 and 60 μ g. per 100 ml. respectively when tested 44 hours after exposure, while one subject had a raised urinary urobilinogen content 7 days after exposure. These findings suggest that changes in normal metabolism may occur following exposure to 49 p.p.m. The CCl4 concentration in expired air was plotted on log.-log, paper against time and was found to decrease exponentially after exposure. The value during the first hour was directly related to the concentration of CCl4 to which the subject had been exposed. The infra-red analysis of CCl4 in expired air was thus shown to be a practical method of estimating the degree of exposure. Samples taken 15 minutes or more after exposure were more useful than those taken immediately, as contamination with atmospheric CCL vapour may occur in the latter case.

The present data are applicable only to exposures to CCl₄ lasting one to 3 hours. Further experiments with

animals exposed for various time intervals and correlatration. The determination of lead in a single specimen, tion of the results with the data obtained from human subjects are desirable.

1023. The Distribution and Excretion of Inhaled Mercury

British Journal of Industrial Medicine [Brit. J. C. GAGE. J. industr. Med.] 18, 287-294, Oct., 1961. 4 figs., 11 refs.

In these investigations of the distribution and excretion of inhaled mercury vapour, which were carried out atthe research laboratories of a large chemical firm, albino female rats were used throughout. In the first experiment 12 rats were exposed for 24 hours a day for 28 days to mercury vapour in a concentration of 1 mg. per c.metre.. The rats survived but lost weight, became lethargic, and showed slight tremors, especially when lifted by their tails. In the second series 6 rats were given repeated continuous exposures to the same concentration of mercury vapour for 100 hours from Monday to Friday in each week for 6 successive weeks. As a result growth was retarded, they appeared lethargic and squeaked when touched, and after 5 weeks these rats also showed fine tremors when lifted by their tails. In the last test. in which 6 rats were exposed to mercury vapour (concentration as before) for 7 hours a day on 5 days a week for 18 successive weeks, the resulting symptoms were similar to those in the first and second experiments but appeared more slowly, the only other difference being that the rats showed a slight increase in weight during the period.

It was found that in all the experiments the tissues reached a saturation point, though the urinary excretion rate was not constant following the cessation of inhalation of mercury vapour. The lungs cleared fairly rapidly, there was slower clearance from the kidneys, while the brain retained some mercury the longest. The author has calculated that if the results obtained in rats in these. experiments with mercury vapour at 1 mg. per c.metre can be applied to man breathing 10 c.metres a day for 5 days with the maximum allowable concentration of mercury vapour of 0.1 mg. per c.metre then the daily absorption might be expected to be about 500 μ g., with a total excretion over 7 days of approximately 2.5 mg. If the total exposure were short the bulk of the mercury would be eliminated in a few days, but if exposure continued for several weeks the resulting accumulation of mercury would be excreted for a considerable time and could amount to several hundred μg , per day.

Anne Tothill

1024. The Toxicity of Precipitated Silica P. D. Byers and J. C. GAGE. British Journal of Industrial

Medicine [Brit. J. industr. Med.] 18, 295-302, Oct., 1961. 5 figs., 13 refs. In this experimental study of the effect of inhaled

silica, reported from the Postgraduate Medical School of London, groups of 50 male and 50 female adult rats were injected intratracheally under light ether anaesthesia with 1 ml. of a 2.5% suspension of three different. samples of sterile precipitated silica of which the particle sizes were 19, 60, and 25 mu respectively. It was found that doses higher than 25 mg. caused death within 24 hours. All rats received the precipitated silica of particle

size $60 \text{ m}\mu$ and all initially tolerated the dose well, but 12 of the group died within 4 days and post mortem showed signs of consolidation and abscess formation in the lung. In all further experiments 2,000 units of penicillin was included in the first injection and no further infections occurred. At 3 intervals during the 12 months after injection 5 male and 5 female rats were killed and the silica content of the lungs, liver, kidneys, and spleen was determined. Similar groups were killed for histopathological examination of the lungs.

The histological distribution of silica in the lungs was not uniform but occurred in small areas throughout one or both lungs, with occasionally a large amount deposited in one lung segment. The three dusts elicited the same response in both male and female animals. The silica particles were seen to be contained within macrophages which were aggregated into foci around terminal and respiratory bronchioles. When the deposition of dust was very heavy the lung structure was completely obliterated by contiguous lesions of macrophages, fibroblasts, and lymphocytes which appeared 12 weeks after injection. After some time, however, the lesion became smaller and some contraction of the lung occurred. There was little evidence that the lymphatic system played any part in dust elimination. It was noted that the nature of the lesion was related to the type of dust used, dust with a particle size of 25 mu being the most quickly eliminated and the 60-mu size the slowest; the latter size also caused the largest lesions to develop. In general the effect of the dust on lung function appeared to be small. There was mild emphysema in a few lungs and apart from a few large abscesses and foci of bronchiectasis there was little evidence of infection, though of course these animals were protected with penicillin. The authors do not consider that the presence of dust in the lungs greatly influences the course of lung infection—a view confirmed by examination of 10 normal adult male and female rats in whose lungs microscopic and macroscopic inflammatory lesions were present with a similar over-all frequency as in the lunes of the experimental animals

wheat seeds treated with the fungicide mixed with untreated wheat. After 10 days he noticed severe pain in both knees and 10 days later he developed generalized deep-seated pains, followed at 3 weeks by pruritus of the soles, palms, and genitalia and accompanied by affected vision. He had some oliguria and a cough with mucoid sputum. Some 2 months after the onset of symptoms he was admitted to hospital, being then thin and in pain, and examination showed a grey zone on the 2 lower incisors and coarse twitchings in the limb. muscles.1 There was excitability and tenderness of muscles which did not follow the course of the nerves. All other systems were normal. The second patient was a male aged 16 who, 6 weeks after he had eaten bread made from treated wheat, developed abdominal pain, headache, weakness of the legs, unsteadiness when standing, and progressive deterioration of vision accompanied by polydipsia and polyuria; his 2 brothers were similarly affected. On admission, 2 weeks after the initial symptoms, he was thin and almost blind, but mentally clear. He had slurred speech with marked ataxia. There was temporal pallor and some spasticity of the lower limbs and the reflexes were diminished but " flexor. The urine showed a trace of albumin and contained granular casts. The electrocardiogram indicated a shifting pacemaker; no other abnormality was found. This patient was treated with dimercaprol (BAL) for 5 days and his vision and gait markedly improved.

The authors then review 26 further cases seen by them personally, in which the duration of symptoms and signs was from 5 to 120 days. Of these patients 14 had polyuria and 2 oliguria, 9 vomiting, 7 diarrhoea, 5 constipation, 15 abdominal pain, 10 skeletal pain, 20 inability to walk, 14 ataxia, one drowsiness, 8 impaired vision, 3 tremor, 6 twitchings, 5 change of mentality, 6 pruritus, 14 increase in tendon reflexes, 2 absence of tendon reflexes, 5 loss of abdominal reflexes, and 11 had an extensor plantar response. Electrocardiograms, recorded in 15 patients, showed cardiac damage in 9.—The natients were treated with senditives analogues.

Radiology

1027. The Lower Oesophageal Ring. (Der untere Osophagusring)

H. KLEINFELDER and F. LONGIN. Fortschritte auf dem Gebiete der Rönigenstrahlen und der Nuklearmedizin [Fortschr. Rönigenstr.] 95, 610-623, Nov., 1961. 7 figs., 19 refs.

The concept of the lower oesophageal ring originated with the work of Schatzki and Gary (Amer. J. Roentgenol., 1953, 70, 911). This condition is characterized by a particular type of dysphagia and an annular narrowing of the oesophageal lumen at the gastro-oesophageal junction; it is thought to be associated with a small hiatus hernia. The present authors, from the Medical Polyclinic of the University of Würzburg, report their own observations in 2 cases in which a lower oesophageal ring was associated with dysphagia. They conclude that the ring in question corresponds with the so-called "middle ring" of Hafter (Radiologe, 1961, 1, 141; Abstr. Wld Med., 1962, 31, 79). F. M. Abeles

1028. Changes in the Lumbar Cerebro-spinal Fluid during Air-encephalography

D. MARRACK, V. MARKS, and R. S. C. COUCH. British Journal of Radiology [Brit. J. Radiol.] 34, 635-639, Oct., 1961. 3 figs., 15 refs.

This paper from the National Hospital, Queen Square, London, describes the changes in composition of the cerebrospinal fluid (C.S.F.) which occur during air encephalography and discusses the likely reasons for these changes. Observations were made on C.S.F. from 85 consecutive patients undergoing air encephalography. The first specimen in each case was collected as soon as the lumbar puncture was performed and before any air had been introduced; the second consisted of all the C.S.F. which was collected after the introduction of air approximately 30 minutes after the first specimen was taken. The two specimens were examined in the laboratory by routine methods.

It was discovered that in 78 out of 81 cases the protein concentration fell between the first and second specimens by a mean value of 11 mg. per 100 ml. In only 3 cases was the protein concentration higher in the second specimen. The glucose concentration was estimated in 37 cases, and no significant difference was found between the first and second specimens, so that this aspect of the investigation was discontinued. The cell count was often found to be significantly higher in the second specimen, the cells being almost exclusively mononuclear in type.

It is recognized that there are in healthy subjects a lower concentration of protein and a lower cell count in the ventricular as compared to the lumbar C.S.F. The outflow of C.S.F. from the ventricles during encephalography could account for the fall in protein concentration, but it is felt that the increase in cell count can be

accounted for only by the desquamation of arachnoid cells. The change takes place too quickly to be accounted for by inflammatory changes, and, moreover, the cells are not of the right type to be produced by an inflammatory reaction. The C.S.F. obtained at air encephalography is thus shown to be unsuitable for laboratory estimation of the components of a patient's lumbar C.S.F.

Arnold Appleby

1029. Anglocardiographic Determination of Left Ventricular Volume. [In English]

H. ARVIDSSON. Acta radiologica [Acta radiol. (Stockh.)] 56, 321-339, Nov., 1961. 10 figs., 18 refs.

Biplane angiocardiography was used to determine left ventricular volume in different phases of the heart cycle. The stroke volume in the left ventricle was determined from the maximum and minimum left ventricular volumes, and the minute volume during angiocardiography was then determined from the stroke volume and cardiac rate. The minute volume determinations at angiocardiography and by Fick's technique were compared.—
[Author's summary,]

1030. Arterlosclerotic Narrowing of Renal Arteries Associated with Hypertension

D. A. VAN VELZER, C. H. BURGE, and G. C. MORRIS JR. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 807-818, Nov., 1961. 15 figs., 32 refs.

The relationship between arteriosclerotic narrowing of the renal arteries and hypertension was studied at the Methodist Hospital, Houston, Texas, in 1,332 aortograms. Translumbar aortic puncture was performed with the tip of the needle above the coeliac axis, after which 10 to 25 ml. of 70% "urokon" was injected manually or with an automatic injector, the radiograph being exposed near the end of the injection. Only 25 ml. of contrast material was injected on any given-day since impaired renal function or even death might result from excessive amounts. In most of the patients aortography was performed because of aneurysm or occlusive disease in the abdominal aorta. Thus most of the patients had advanced arteriosclerotic disease and relatively few of the examinations were undertaken primarily for the evaluation of hypertension. Renal artery anomalies were noted and kidney size and renal function were estimated by pyelography. Arteriosclerotic disease of the abdominal aorta and other branches was also noted. The average age of the patients examined was 55 years.

Of the 1,332 aortograms 437 were considered to be unsatisfactory, the renal arteries being inadequately visualized, mainly because the puncture was below the origin of the renal arteries; in a further 74 cases no blood pressure readings were taken. There were thus 821 aortograms available for analysis. It is pointed out

that the criteria for hypertension will-greatly affect the results. A diastolic reading over 90 mm. Hg was considered to be abnormal at any age, while the baseline for the systolic pressure was taken from insurance company statistical analyses. Under 40 years of age 140 mm. Hg was regarded as the dividing line between normotension and hypertension, with an addition of 5 mm. Hg for each succeeding decade. Of the 821 patients 78.3% had hypertension. Narrowing of one or both renal arteries was present in 50.7% and both renal artery stenosis and hypertension were present in 43.7%. In an overwhelming majority of cases excretion of contrast material and kidney size at pyelography were normal. The authors consider that excretion pyelography following aortography adds very little to the evaluation of the blood supply to the kidneys. John H. L. Conway-Hughes

1031. The Value of Gas Distension of the Stomach in Urography for Diagnosis of Developmental Defects of the Upper Urinary Tracts in Children. (Значение выполнения жилудка газом с одновременной урографии для расповназания пороков развития верхних мочевых путей у детей)

K. Kozlovskii. *Педиатрия* [Pediatrija] 40, 46–48, Nov., 1961. 1 fig., 4 refs.

Intravenous pyclography in young children is difficult owing to gas shadows in the bowel, and good visibility of the upper parts of the urinary tract is obtained in only some 35% of cases. However, distension of the stomach with gas presses the intestines downwards and gives a uniform foreground to the pelvic shadows. For this procedure the author employs a technique which he finds very reliable. The child is given a semi-fluid diet on the previous day, and is kept fasting from midnight (or from 3 a.m. in the case of a young infant). Next morning he is given the contrast medium (20 to 40 ml. of 45% "pelviran") and immediately drinks 50 to 200 ml. of aerated water; 5 minutes later the first pyelograms are taken. This technique is effective for children up to the age of 10 years, but after that the results are less satisfactory, since the oesophagus extends down to the level of the renal pelvis on the right side.

L. Firman-Edwards

RADIOTHERAPY

1032. Results of Radiotherapy of Carcinoma of the Lip, 1945-60. (Ergebnisse der Strahlenbehandlung des Lippenkarzinoms in den Jahren 1945 bis 1960)

G. BARTH and W. KERN. Strahlentheraple [Strahlentherapie] 116, 203-213, Oct. [received Dec.], 1961. 39 refs.

This is a report of the results in 78 patients (including 12 females) who were treated at Erlangen University Medical Clinic for carcinoma of the lip during the period 1945–60. The patients were drawn from a mainly rural population and therefore included a relatively high proportion of advanced lesions. Treatment in almost all cases was by Chaoul short-distance x rays. Secondary nodes were present in 15 cases at the beginning

of treatment and appeared later in a further 10. Doses of usually 500 to 600 r. were given to a minimum total of 5,000 r. In 66 patients with cancer of the lower-lip, the symptom-free results were: 50 well at 3 years (75.7%), 45 at 5 years (63.8%), and 15 at 10 or more years. Of 12 with cancer of the upper lip 8 were well at 3 years (66.6%) and 7 well at 5 or more years (58%). The combined results were: 58 well at 3 years (75.6%) and 52 well at 5 years (66.6%).

On the basis of animal experiments, the optimum interval between doses is thought to be 48 hours, rather than the conventional 24 hours. Of 23 patients so treated 20 were well at 5 years (87%)—a suggestive but not statistically significant result. Secondary nodes were treated mostly by deep x rays (H.V.L. 1 05 mm. Cu), sometimes followed by surgery. Prophylactic radiation is considered unwise. A table is given of the results reported by 30 authors between 1884 and 1960, including those in cases treated by surgery; the latter usually produces a 3-year symptom-free rate of not more than 60%, though a high proportion of advanced cases is generally involved.

J. Walter

1033. Intracavitary Radioactive Colloldal Gold in the Management of Ovarian Carcinoma: Report on 114 Cases Treated with Au^{198}

R. G. Rose. Obstetrics and Gynecology [Obstet. and Gynec.] 18, 557-563, Nov., 1961. 3 figs., 13 refs

This paper reports the results obtained in 114 patients suffering from ovarian carcinoma who were treated with radioactive colloidal gold (198Au) at the M. D. Anderson Hospital and Tumor Institute, Houston, Texas: The 198Au was inserted into the thorax by means of a thoracentesis needle, but into the abdomen with a polythene catheter threaded through a trochar. When no ascites was present peritoneal insufflation with nitrous oxide was employed to ensure that the catheter was in the peritoneal cavity and that no loculation was present.

Of 65 patients with recurrent malignant ascites who were thus treated 42 (65%) showed improvement; of 7 patients with pleural effusion 6 had some benefit, but in one patient with pericardial effusion the response was poor. There were 8 patients with tumour masses but no ascites in the series; none of these developed ascites later and in some cases there was reduction in tumour size. Lastly, of 12 patients with malignant peritoneal seedling deposits 5 are living free of disease 6 to 50 months following treatment. The remaining 24 patients, in whom a malignant ovarian cyst ruptured at operation, were treated prophylactically with 198Au postoperatively; although 18 (75%) of these were still alive 6 to 76 months after treatment, the mean period of follow-up was considered too short to allow of any firm conclusions. Minor complications such as nausea (in 42% of cases), vomiting (30%), and low-grade fever (30%) were encountered. The author suggests that the optimum dose of 198Au in such cases is between 150 and 200 mc. and that this may be repeated once if necessary, but that a third treatment is not worth while and resort may be had to a chemotherapeutic agent such as thioTEPA, which is M. Sutton often of value.

ABSTRACTS OF WORLD MEDICINE

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Pathology

1034. Early Morphological Changes in the Gastrointestinal Tract Due to Polonium Intoxication. (Развитие ранних морфологических изменений желудочнокишечного тракта при введении полония)

G. A. LEBEDEVÁ. Apxus Патоловии [Arh. Patol.] 23, 16-21, No. 3, 1961. 5 figs., 8 refs.

In this experimental study radioactive polonium was administered intravenously to 25 white male rats in a dosage of $0.06\,\mu c$, per g. body weight. The animals were then killed, 3 at a time, 1, 3, 6, 12, 24, 48, and 72 hours later; 4 rats died spontaneously between 13 and 15 days after the administration of polonium. No naked-eye changes were observed during the first 3 days. Microscopically, however, isolated disintegrating cells were noticed as early as 3 hours after injection of the isotope, these being seen mainly in the epithelium of the crypts and in the stroma of the wall of the small intestine. After 6 hours the necrotic process had spread to involve the crypts of the large intestine, the epithelium of the villi, and the cells of lymphoid follicles. The gastric mucosa became involved after 12 hours. Depression of mitotic activity was observed as early as one hour after the injection of polonium, increased during the first 6 hours, and persisted during the whole period of the experiment.

A. Swan

1035. Liberation of Material with Platelet-like Coagulant Properties from Intact Red Cells and Particularly from Reticulocytes

B. A. Bradlow. British Journal of Haematology [Brit. J. Haemat.] 7, 476-495, Oct., 1961. 6 figs., 47 refs.

The results of an investigation carried out at the Postgraduate Medical School of London provide confirmatory evidence that material, probably a phospholipid, is released by normal and abnormal intact, unlysed erythrocytes when incubated at 37°C. in siliconized tubes. Similar material is not liberated by platelets or leucocytes under these conditions, but large amounts are liberated by both erythrocytes and platelets at 4° C. The material can be detected after 30 minutes and release continues for at least 4 hours. Although liberated from mature cells, much larger amounts are released from reticulocytes whether obtained from patients with haemolytic anaemia or with pernicious anaemia during response to therapy. In paroxysmal nocturnal haemoglobinuria the amount released is greater than would be expected from the number of reticulocytes present.

The material causes a pronounced shortening of the fibringen time in the thrombin generation test and in

the "stypven" time. Whether these findings in vitro are paralleled by an increased coagulability of the blood in vivo is uncertain, but there is much clinical evidence of an association between many types of haemolytic anaemia and intravascular thrombosis.

R. B. Thompson

1036. Demonstration of Circulating Antinuclear Globulins in Ukerative Colitis

P. CALABRESI, W. R. THAYER JR., and H. M. SPIRO. Journal of Clinical Investigation [J. clin. Invest.] 40, 2126–2133, Dec., 1961. 2 figs., 33 refs.

The authors, at Yale University School of Medicine, New Haven, Connecticut, investigated the sera of patients with ulcerative colitis for the presence of gamma globulins having an affinity for nuclear material. Their method was to treat alcohol-fixed blood films first with the patient's serum and then with fluorescein-labelled rabbit antihuman gamma globulin, and finally to examine the preparations by fluorescent microscopy.

The sera of 18 out of 24 patients contained such nuclear-combining globulins. In those who had had colectomy they were less frequent (4 out of 13). The number of cases studied was hardly sufficient to establish any significant correlation with various other clinical manifestations, but it was noted that of 8 patients who had had the disease for more than 5 years, all had positive sera compared with 10 out of 16 whose disease was less long-standing. All 4 patients with splenomegaly also had positive sera. There were no positive reactors among patients with carcinoma of the colon (17), amoebic colitis (2), or diverticulosis (2), nor in one case each of schistosomiasis and multiple polyps. A positive result was given, however, by one patient with familial polyposis whose son had ulcerative colitis.

The authors emphasize that it cannot be assumed at present that gamma globulin combining with nuclei is an antibody or that it plays a part in the pathogenesis of ulcerative colitis.

M. C. Berenbaum

1037. A New Blood-group Antigen Present in 80% of White Subjects. (Un nouvel antigene de groupe sanguin érythrocytaire présent chez 80% des sujets de race blanche) C. SALMON, D. SALMON, G. LIBERGE, R. ANDRÉ, P. TIPPETT, and R. SANGER. Nouvelle revue française d'hématologie [Nouv. Rev. franç. Hémat.] 1, 649-661, Sept.-Oct. [received Dec.], 1961. 6 figs., 6 refs.

A new anti-erythrocyte antibody has been identified in a female patient aged 59 named Auberger (Au) who had received multiple transfusions for the treatment of haemorrhages from oesophageal varices. The patient's blood group was O, MNSs, P, CDe/cde, Lu(a-), K-, Kp(b-), Le(a-b+), Fy(a+b-), Jk(a+b+). Her saliva contained H, Le^a, and Le^b substances. Before the development of this new antibody her serum had also contained anti-E, anti-K and anti-Fy^a antibodies, as, well as antileucocyte and antiplatelet agglutinins.

This new antibody, named anti-Au^a, was studied by the indirect Coombs technique. The Au^a antigen is stated to be present in 81 99% of persons of the white race. Extensive genetic studies were carried out at the Central Department of Blood Transfusion, Paris, and the Blood Group Research Unit, the Lister Institute, London. No association was found between Au and the other blood systems. It is therefore likely that a new blood system has been identified—the Auberger system.

A. W. H. Foxell

CHEMICAL PATHOLOGY

1038. An Assessment of Routine Hospital Urine Testing for Protein and Glucose

J. A. KIRKLAND and H. G. MORGAN. Scottish Medical Journal [Scot. med. J.] 6, 513-519, Nov., 1961. 2 figs., 14 refs.

From the University of St. Andrews, Dundee, the authors, commenting on the inefficiency of routine urine testing as carried out in the wards and clinics of a major teaching hospital, describe clinical and laboratory trials of 2 new methods of testing urine for the presence of protein and glucose. These involve the use of paper strips impregnated at one end with a reagent which changes colour when dipped into urine containing protein (" albustix") or glucose ("clinistix"). They also tested "uristix", which has reaction portions for both protein and glucose. For the purposes of the trial 1,033 noncatheter specimens of urine were obtained over a period of 4 months. Patients were not selected and came from 2 male and 2 female wards and from an antenatal clinic. Urines were first tested by the nursing staff and then again in the laboratory on the same morning. Tests used in the wards were: for protein, the heat test, aqueous salicylsulphonic acid test, or albustix; for glucose, "clinitest" tablets or clinistix or both. Those used in the laboratory were the alcoholic salicylsulphonic acid test or uristix (for protein) and clinistix (for glucose).

There were 281 positive results for proteinuria as detected in the laboratory; in the wards 164 of these were detected and 117 missed, and 21 false positive results were obtained. For glycosuria there were 212 positive results as tested in the laboratory; 80 of these were detected in the wards and 132 missed, and there were 14 false positive results. These unexpected large discrepancies led to a more detailed analysis of the results from a study of 505 further specimens of urine.

Whichever method was used in the wards, the results showed a similar degree of accuracy, the only major difference being that in tests for protein fewer false positive results were reported with albustix. In ward testing for glucose, however, clinistix gave a much greater

accuracy than clinitest, detection ranging from 30 to 95% with clinitest to 0 to 23% with clinitest. An incidental finding was the occurrence of heavy proteinuria in patients who had recently had radio-opaque substances injected for aortography, pyelography, or angiography.

The authors consider that the efficiency of ward testing depends on a number of factors, especially the real and continuing interest of the senior medical staff. For instance, during the investigation one unit was given a lecture on the value of glucose detection, with the result that the incidence of correct positive results rose from 40% to 89.6% with the same method, whereas the achievement of the other units remained unchanged.

G. Clayton

1039. Studies on Human Serum β -Lipoproteins, Including their Protein Moiety. [Monograph, in English] K. Cramer. Acta medica Scandinavica [Acta med. scand.] 170, 1–15, 1961. 37 refs.

MORBID ANATOMY AND CYTOLOGY

1040. The Histological Diagnosis of Toxoplasmic Lymphadenitis

A. G. STANSFELD. Journal of Clinical Pathology [J. clin. Path.] 14, 565-573, Nov., 1961. 10 figs., 39 refs.

The author of this paper from St. Bartholomew's Hospital, London, describes 3 cases of toxoplasmic lymphadenitis in which the diagnosis was unsuspected clinically but was established by lymph-node biopsy.

The lymph node in each instance was markedly enlarged, but apart from this there was nothing remarkable about the macroscopic appearance. The author states that on microscopical examination the essential features are those of a subacute to chronic lymphadenitis with well-marked periadenitis. A striking degree of lymphoid hyperplasia is present, and many of the follicles are large and irregular in outline with active germinal centres. There are numerous mitoses of regular pattern in the germinal centres and many karyorrhectic necrotic cells. Scattered through the pulp of the node there are small clusters of very conspicuous, pale-staining histiocytes. These resemble the epithelioid cells of tuberculosis, but multinucleate cells are scarce and Langhans's cells and caseation are absent. The cell clusters are smaller and less sharply defined than in sarcoidosis and there is no related reticulin. Almost as distinctive a feature as the histiccyte clusters is the dense packing of many of the lymph sinuses with free macrophages, usually small but often laden with cellular debris. Lastly, there is a marked increase of plasma cells throughout the pulp of the node.

A cyst was found in one of the 3 cases, otherwise no definite organisms were observed. The cyst was located, apparently extracellularly, at the margin of a lymph follicle. It was oval, with a definite eosinophilic external limiting membrane, and contained many very small toxonlasms.

It is pointed out that while it is exceedingly rare for toxoplasmic cysts to be found in lymph nodes, the histology is, in many instances, sufficiently distinctive for a tentative diagnosis of toxoplasmic lymphadenitis to be made on lymph-node biopsy. The diagnosis should always be confirmed by isolation of the parasite or by serological tests.

H. Caplan

1041. Amyloidosis: Appraisal of Intubation Biopsy of the Small Intestine in Diagnosis

P. A. Green, J. A. Higgins, A. L. Brown Jr., H. N. Hoffman, and R. L. Sommerville. Gastroenterology [Gastroenterology] 41, 452–456, Nov., 1961. 19 refs.

By means of a Crosby capsule peroral intubation biopsy of the small intestine was carried out in 6 cases of amyloidosis showing no significant gastro-intestinal symptoms. Microscopical examination of the specimens thus obtained showed definite evidence of amyloidosis in 5 of these cases. From this the authors, who report from the Mayo Clinic, Rochester, Minnesota, conclude that intubation biopsy is a useful diagnostic method in cases of suspected amyloidosis.

J. B. Wilson

1042. On the Development of Foci of Extramedullary Haematopolesis at the Sites of Tissue Damage in Leukaemia. (С развитии очагов экстрамедуллярного кровотворения на местах повреждения тканей при лейковах)

A. K. AGEEV. Apxus Патоловии [Arh. Patol.] 23, 50-55, No. 8, 1961. 4 figs., 11 refs.

Histological examination of the cutaneous and subcutaneous lesions, especially those at the sites of drug injections, in a series of 27 necropsies on patients dying of leukaemia (acute myeloid in 18 cases, chronic myeloid in 4, and chronic lymphatic in 5), led the author to the following conclusions. In all cases in which the injections were administered more than 3 days before death foci of "extramedullary haematopoiesis" were found at the sites of injections. From the description given it would appear that these foci were actually localized centres of leukaemic proliferation. Erythropoietic elements were present in such foci only in the cases complicated by haemolytic anaemia, the antibodies being demonstrable by the Coombs test. In infected lesions, especially those with ulceration, the presence of a considerable accumulation of neutrophil granulocytes was observed in a case of acute myeloid leukaemia, in spite of the fact that their number in the peripheral blood was very low (128 per c.mm.). Foam cells, which are very common at the sites of injections in non-leukaemic cases, were found in this series in only 3 cases in which haematopoiesis was depressed by treatment with a cytotoxic drug.

1043. Peculiarities of Morbid Anatomy of Acute Leukaemia in Children. (Особенности патологической анатомии острых лейковов у детей)

T. E. IVANOVSKAJA. Архив Патоловии [Arh. Patol.] 23, 58-63, No. 11, 1961. 6 figs., 22 refs.

This paper is based on a study of 50 cases of leukaemia in children aged from 3 to 12 years, of whom 43 had acute leukaemia, the subacute and chronic forms being present in only 7. The most common type (19 cases) was a poorly differentiated "stem-cell" leukaemia—haemo-

cytoblastosis. A wide dissemination of the process with involvement of many organs was typical, contrasting with the more localized forms in adults. Acute myeloid leukaemia was the next commonest (17 cases). Boys were affected to a greater extent than girls, 33 of the 43 patients with acute leukaemia being males. Prolongation of life for periods of up to 2 years was achieved by means of hormonotherapy.

The author postulates the presence of an excess of somatotrophic hormone in children who develop leukaemia and cites in support of this theory the following observations: (1) the patients were predominantly children of athletic build, with pronounced facial features; (2) congenital leukaemia is commoner among large babies (birth weight 4 to 4.5 kg.); and (3) in some cases of acute leukaemia, hyperplasia of eosinophil cells of the pituitary was found. The thymus gland, in those cases in which leukaemic infiltration of this organ was absent, showed involutionary changes and a reduction in weight down to one-third of normal, with disappearance of the thymocytes, whereas Hassall's corpuscles were hypertrophied.

A. Swan

1044. Microscopic Properties of the Basement Membrane and Elastic Fibers of Trachea and Bronchus of Smokers and Nonsmokers

Y. HAYASHI, E. V. COWDRY, and V. SUNTZEFF. *Cancer* [Cancer (Philad.)] 14, 1175–1182, Nov.-Dec., 1961. 7 figs., 36 refs.

A histological study of the trachea and bronchus in smokers and non-smokers, white males aged 40 to 77 years, most of whom died from myocardial infarction, is reported in this paper from Washington University School of Medicine, St. Louis, Missouri.

The elastic fibres of trachea and bronchus in most nonsmokers are relatively straight and regular, deeply coloured, and generally show an even thickness and stainability. No significant difference between minimum smokers (fewer than 20 cigarettes a day) and non-smokers is demonstrable. In the present series half of the moderate smokers (20 cigarettes a day for 20 years) had irregularly wavy elastic fibres. Considerable changes in the elastic tissue were found in heavy smokers (20 to 60 cigarettes a day for 20 or more years). In most of these there was an increase in the amount of elastic fibres and irregular waviness, thickness, and stainability of these fibres. The changes were not related to age.

The basement membrane of smokers was generally thicker than that of non-smokers. The average maximum thickness of the membrane of the trachea and bronchus appeared to increase with smoking, but the differences were not formally significant statistically. Epithelial metaplasia seemed to have some relationship to thickening of the basement membrane. In general, where there were some small areas of stratified squamous epithelium there were also very thick basement membranes.

It is concluded that smoking, especially for long periods, causes alterations in elastic fibres. These changes are responsible for some loss of elasticity in the trachea and bronchus.

H. Caplan

1045. The Renal Complications of Diabetes Mellitus: Needle Biopsy Study of the Renal Histopathology M. S. Sabour, M. N. El Mahallawy, and I. Abou-El-Naga. Scottish Medical Journal [Scot. med. J.] 6, 495–512, Nov., 1961. 23 figs., 25 refs.

Renal histopathology was studied in 75 diabetic patients, 19 of whom showed clinical nephropathy, while the others had no clinical evidence of renal affection. Needle biopsy of the kidney was used and the aim was to detect very early diabetic renal changes and to try to follow the evolution of the well-known advanced lesions. In addition 11 normal and 110 pathological but non-diabetic renal biopsies were studied in the same way in order to investigate the specificity of the diabetic lesions.

The renal lesions found in diabetes were the following: (1) Glomerular: dilatation of the capillaries and increased size of the glomeruli; thickened basement membrane of Bowman's capsule and capillaries; capillary microaneurysms; diffuse glomerulosclerosis; nodular glomerulosclerosis; hyaline fibrinoid lesions. (2) Tubular: thickened basement membrane; deficient or interrupted brush border; glycogen, lipoid and hydropic vacuolization of cells; hyaline fibrinoid lesions. (3) Vascular: atheroma of the renal arteries; arteriolosclerosis; venosclerosis. (4) Interstitial tissue: oedema; excess connective tissue; cellular infiltration.

The lesions of diffuse and nodular glomerulosclerosis were found to be carbohydrate in nature, probably a mucopolysaccharide similar to the ground substance, derived from the thickened basement membrane; and these mature to form collagenous tissue. The hyaline fibrinoid lesions appeared to be lipoid in nature, occurring inside capillaries as lipoid plugs or emboli, in glomeruli previously the seaf of sclerosis.—[Authors' summary.]

1046. Glomerulonephrosis in Cirrhosis of the Liver. (Über Glomerulonephrose bei Lebercirrhose)
H. Meister. Frankfurter Zeitschrift für Pathologie
[Frankfurt. Z. Path.] 71, 348-355, 1961. 1 fig., 41 refs.

In an attempt to define the pathological basis of renal failure in patients with severe liver damage—the hepatorenal syndrome—the author, working at St. Georg Hospital, Leipzig, studied sections of the liver and kidneys from 85 cases of cirrhosis of varied actiology and 40 controls without hepatic or renal disease. Sections were stained by the method of van Gieson and periodic-acid—Schiff (P.A.S.) and frozen sections, were Sudan-stained.

The salient finding was widening of the mesangium of the glomerular vessels, producing a focal band-like or patchy or brush-like appearance, which in the most severe cases extended diffusely throughout the glomerulus. Whereas in a normal glomerulus the capillary basement membrane of the tuft is represented by fine P.A.S.-positive-staining lines, there were here purple bands, trabeculae, and rings. This change was focally distributed in 24 cases and diffusely in 6. In a further 3 cases, which were definitely not diabetic, there was focal club- or disk-like condensation of the mesangium, which was indistinguishable from diabetic glomerulo-sclerosis. In recent cases this stained well, like the other

thickenings, with P.A.S., but in long-standing cases it stained better by van Gieson's stain than with P.A.S. To be of significance the widening of the mesangium must be generalized and considerable, since mild degrees of it were seen also in arterio- and arteriolo-sclerosis. There was no definite correlation between the cause of the cirrhosis and the renal mesangial thickening, but the severity of the hepatic changes was related to the renal pathology. Early cirrhosis was never accompanied by renal damage. Increased cellularity of the glomerulus was noted in about half the cases, but this was generally only moderate and no leucocytes were seen.

Another striking finding observed in 18 of the 85 cases of hepatic cirrhosis was a fatty change in part of the renal tubular epithelium; it was severe and generalized in 5 of these, again proven non-diabetics. Of these 18 patients, 5 had died in hepatic failure. Among other observations briefly mentioned was the finding in some cases of a protein precipitate in the capsular space, with thickening of Bowman's capsule and periglomerular fibrosis. Hyaline casts were found in 50% of the cirrhotic cases, but also in 30% of the controls. The author argues against the designation "membranous proliferative glomerulonephritis", but supports rather Fahr's and Randerath's term glomerulonephrosis. He considers the thickening of the glomerular basement membrane and the fatty tubular change to be due to a disturbance of protein and lipid metabolism consequent upon hepatic failure.

1047. The Pathologic Spectrum of Huntington's Chorea W. T. E. McCaughey. Journal of Nervous and Mental Disease [J. nerv. ment. Dis.] 133, 91-103, Aug. [received Nov.], 1961. 6 figs., 19 refs.

Contributors to the literature on Huntington's chorea have described lesions in the striatum (caudate nucleus and putamen) and in the third, fifth, and sixth layers of the cerebral cortex, the thalamus and subthalamic areas, and the dentate nucleus of the cerebellum. In this paper from the Mayo Clinic a pathological study is reported of the nervous system of 21 patients with Huntington's chorea. The ages of the patients ranged from 36 to 77 years and the duration of symptoms from 7 to 26 years.

Striatal degeneration characterized by diffuse loss of small ganglion cells and marked reactive astrocytosis was invariably the dominant lesion. The caudate nucleus and putamen were similarly involved, although the former was more affected than the latter. The globus pallidus often showed a mild or moderate secondary atrophy without evidence of loss of nerve cells. Less often similar changes were noted in the anteromedian nucleus of the thalamus. Gyral atrophy might be pronounced or slight, and the microscopic changes in the cerebral cortex varied accordingly, but were always mild compared with the striatal region. The cortical degeneration closely resembled that seen in simple senile atrophy. The dentate nucleus showed an obvious loss of nerve cells in 9 cases and in 3 this was conspicuous. In 2 cases there was marked atrophy of the nuclei pontis. The rest of the body showed no evidence of any underlying systemic disturbance. R. Wyburn-Mason

Pharmacology and Therapeutics

1048. Norandrostenolone Decanoate—a New Anabolic Steroid with Prolonged Effect: Some Clinical Observations. [In English]

J. L. KALLIOMÄKI, T. K. MARKKANEN, A. M. PIRILÄ, and I. RUIKKA. Annales medicinae internae Fenniae [Ann. Med. intern. Fenn.] 50, 177–184, 1961. 14 refs.

Norandrostenolone decanoate is a new ester of an anabolic steroid of established repute; given intramuscularly it is effective for at least 3 weeks. In a trial at the Municipal Geriatric Home, Turku, Finland, 15 elderly female patients were given 100 mg. of the ester intramuscularly after an 8-day observation period and were followed up for 30 days. A "double blind" technique was used, another 15 patients being given saline and acting as controls.

The treated group showed a gain in body weight of 2.0 ± 0.28 kg. by the 26th day after injection. Their speed of psychomotor reaction was significantly increased, but they had no significant change in muscle power; neither was there any change in serum cholesterol level, urinary excretion of creatine, creatinine, or riboflavin, or in the results of the urine Sulkowitch test. Psychic stimulation was observed in 12 of the 15 treated patients, and in 3 of these cases this amounted to clear euphoria.

T. B. Begg

1049. Contribution to the Mode of Action and Indications for Treatment with Persantin. (Beitrag zum Wirkungsmechanismus und zur Indikationsstellung einer Persantinbehandlung)

H. HAMMERL and H. SIEDEK. Wiener klinische Wochenschrift [Wien. klin. Wschr.] 73, 788-790, Nov. 10, 1961. 1 fig., 12 refs.

At the Wilhelminenspital, Vienna, the authors have investigated the effect of "persantin" on the transient rise of serum transaminase activity previously observed when fever was artificially induced in patients with overt electrocardiographic (ECG) evidence of coronary insufficiency. Because the enzyme activity falls to the original level after 10 hours in all cases, they consider that the increased transaminase activity in these circumstances is due not to necrosis of heart muscle, but to disturbed cellular metabolism of the already ischaemic heart muscle in the presence of an increased oxygen demand.

Lipopolysaccharide from Salmonella abortus equi or a plant preparation, RF 2077, was given as a pyrogen to 15 fasting petients after a blood sample had been taken to determine the initial level of serum glutamic-oxalacetic transaminase (S.G.O.T.) activity. Further blood specimens were taken after 1, 2, 4, 6, 8, and 10 hours. Three to 5 days later fever was again induced and one ampoule [dose not stated] of persantin was given intravenously an hour later, the S.G.O.T. levels being estimated as before. All the patients had ECG changes at rest in the form of a trough-like depression of the S-T

segment in Lead I and sometimes also in other standard and chest leads. In the first experiment the average initial level of S.G.O.T. was 26 units (range 24 to 32 units) and it rose to 141 units (range 96 to 260 units) after the induction of fever. When persantin was nijected an hour after the pyrogen, however, the enzyme level rose to an average of only 74 units (range 52 to 128 units), the average initial level before the second induction of fever being again 26 units (range 24 to 30 units).

It is suggested that these results indicate that persantin enhances the blood supply and improves the metabolism of the cardiac tissue. The authors have treated 200 cases of angina pectoris with intravenous persantin (1 or 2 ampoules), with relief of the pain in a few minutes in nearly every case. Good results have also been obtained with persantin by mouth for maintenance therapy in uncomplicated cases of angina (especially angina of effort) and after myocardial infarction. However, they consider that parenteral persantin is not advisable in cases of acute myocardial infarction with a systolic blood pressure below 100 mm. Hg because the vasodilatation caused by persantin may result in deterioration of the clinical condition.

1050. The Effect of Digitalis on the Cardiac Output of the Normal Heart at Rest and during Exercise

T. RODMAN, C. A. GORCZYCA, and B. H. PASTOR. Annals of Internal Medicine [Ann. Intern. Med.] 55, 620-631, Oct. [received Dec.], 1961. 6 figs., 40 refs.

The authors report an investigation carried out at the Veterans Administration Hospital, Philadelphia, into the effect of digitalis on the normal human heart at rest and after exercise. In the 33 healthy men aged 20 to 47 years studied cardiac output was measured by an indicator dilution technique following injection of indocyanine green into a catheter in the superior vena cava, blood samples being obtained by a constant flow system from the brachial artery, in which the dye concentration was determined and dilution curves constructed. Oxygen uptake, carbon dioxide output, respiratory quotient, and basal metabolic rate were also measured, all determinations being made both at rest and during a steady exercise state. Similar studies were performed after administration of digoxin, given by mouth to 13 subjects (Group 1) over 5 to 7 days and by intravenous infusion over 2 hours in the other 20 (Group 2). Of the latter group, 6 did not perform the exercise but were examined frequently for 90 minutes following digitalization, when the resting cardiac output was measured.

No significant effect on the resting or exercise cardiac output was observed in Group-1 patients who were slowly digitalized, but in Group 2 given lanatoside C intravenously there was a small but significant reduction in cardiac output at rest. This began to appear as early as 10 minutes after the intravenous injection and reached

its maximum fall (20% of the predigitalization level) at one hour; there was then a return to normal within 2 hours. The response of the heart to exercise after intravenous digitalis was normal. The authors suggest that the small fall in cardiac output observed was most probably due to extramyocardial factors. The normal response to exertion, the rapid onset of the fall in cardiac output, waning of the effect as the peak action of digitalis on the myocardium was obtained, and the lack of a fall in output after oral digitalis all support a non-cardiac cause. They therefore conclude that there is no evidence of any deleterious effect of digitalis, whether given orally or intravenously, on the normal myocardium.

A. E. Read

1051. Studies on a New Intramuscular Haematinic, Iron-Sorbitol

S. LINDVALL and N. S. E. ANDERSSON. British Journal of Pharmacology and Chemotherapy [Brit. J. Pharmacol.] 17, 358-371, Dec., 1961. 10 figs., 25 refs.

Studies relating to the chemistry, absorption, diffusion, and excretion of a new intramuscular iron-sorbitol preparation are reported from Centrallasarettet, Danderyd, Sweden. The preparation was compared with iron-dextrin and iron-dextran.

Saline and serum dilution studies indicated the stability of iron-sorbitol, which was more hypertonic than irondextran. Unlike iron-dextran, iron-sorbitol was neither haemolytic nor did it prolong the blood-clotting time in vitro or in vivo in physiological doses. The absorption was studied by estimating the residual iron content in rabbit gluteal muscle and by following the serum iron levels in both rabbit and man. Two-thirds of the iron was removed from the muscle within 3 hours with ironsorbitol, compared with only 10% with iron-dextran; most had been absorbed in 12 hours with the former and 48 hours with the latter preparation. Serum iron levels were at a maximum in 20 minutes with iron-sorbitol and in 3 hours with iron-dextran. The increased rate of absorption of the iron-sorbitol was attributed to several factors—the low molecular weight, its stability in tissue fluids at a physiological pH, and its absorption into the blood stream both directly and via the lymphatic vessels, whereas iron-dextran is absorbed by the latter route alone. Complete saturation of transferrin, confirmed experimentally, developed in 30 minutes to 6 hours afterintramuscular injection of iron-sorbitol; intravenous injection showed that the iron-sorbitol was removed from the blood in 6 hours, whereas iron-dextran took much longer. The rapid clearance was due to a combination of glomerular filtration of the small molecules and removal by the reticulo-endothelial system; saturation of the iron-binding capacity of the serum is due to reaction between the low-molecular-weight dialysable fraction and transferrin, which renders the iron available for immediate erythropoiesis. Diffusion into tissue fluids, assessed via mouse peritoneum, was similar with both iron-sorbitol and iron-dextran. Renal excretion following intramuscular injection of iron-sorbitol containing 25 to 100 mg. of iron was maximal in the first few hours and attained approximately 30% of the dose in 24 hours. Gerald Sandler

1052. A Comparison of Various Expectorant Drugs Employing a New Method for Determining Sputum Viscosity S. W. Simon and G. A. Harmon. *Journal of Allergy [J. Allergy]* 32, 493-500, Nov.-Dec., 1961. 3 figs., 8 refs.

At the Allergy Clinic of the Brown General Hospital and Veterans Administration Center, Dayton, Ohio, the 24-hour sputa of 27 patients with chronic bronchitis, asthma, or emphysema were collected before and again after a one-week treatment period, during which the patients received either 500 mg. of ammonium chloride 4 times daily, 400 mg. of potassium iodide 3 times daily, or 4 tablets of a preparation containing trypsin and chymotrypsin. The sputa were homogenized in an electric mixer and the viscosity determined with an Ostwald viscometer. No significant change in viscosity was seen after treatment, although potassium iodide and they enzyme tablets did reduce the viscosity slightly. The total amount of sputum did not increase.

[The abstracter wonders whether, if the dose of potassium iodide had been 1 g., the result would have been the same.]

H. Herxheimer

1053. Antitussive Action of L-Propoxyphene in Citric-acid-induced Cough Response

B. CALESNICK, J. A. CHRISTENSEN, and J. C. MUNCH. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 560-564, Nov., 1961. 3 figs., 6 refs.

The antitussive qualities of L-propoxyphene were studied at Hahnemann Medical College, Philadelphia, Pennsylvania. Coughing was produced in 70 healthy adults by a single deep inhalation of a spray of nebulized 25% citric acid solution at each hour for 4 hours after taking by mouth a placebo, or 15 mg. of codeine sulphate, or 15, 25, or 50 mg. of L-propoxyphene, the number of coughs being recorded. The two smaller doses of L-propoxyphene caused a slight diminution in the number of coughs at the end of the first hour, but this effect almost disappeared by the 4th hour. The effect of the 50-mg. dose was almost the same as that of the codeine sulphate in magnitude and duration. There were no side-effects.

1054. Clinical Experience in the Treatment of Oedema with Hygroton. (Klinische Erfahrungen bei der Behandlung von Ödemkranken mit Hygroton)

E. GLASER and S. Rust. Therapie der Gegenwart [Ther. d. Gegenw.] 100, 545-560, Nov., 1961. 6 figs., 18 refs.

From the Regional Hospital, Perlach, Munich, the authors report a trial of "hygroton" (chlorthalidone) in the treatment of 43 patients, of whom 38 had congestive cardiac failure, 4 cirrhosis of the liver, and one nephrosis. The largest single dose given was 400 mg., while for courses the total dose ranged from 150 to 6,500 mg.

In most cases diuresis occurred within a few hours and lasted for 48 to 72 hours. The urinary excretion of sodium and chloride was increased in equimolecular amounts. There was only a slight increase in urinary potassium excretion, and this mostly in the patients with cirrhosis of the liver. There was no increased sensitivity to cardiac glycosides. The serum non-protein nitrogen level rose in 29 out of 41 patients, but returned to normal

values within one or 2 weeks after cessation of treatment. In 7 out of 9 patients with hypertension the blood pressure was reduced to normal levels for 3 to 8 days. In 2 cases there was no response to the drug and in a further 4 the oedema was not completely controlled by hygroton. The authors warn against attempts at forcing diuresis by massive dosage in such cases. They suggest that treatment should be started with a test dose of 100 to 200 mg. and this dose repeated or doubled within the next 24 hours if satisfactory; it should then be continued every other day until cessation of the diuretic effect.

R. Schneider

1055. A Pharmacological Investigation of the Hypnotic Action of a New Derivative of Chloral Hydrate, Chlorhexadol

G. A. CONDOURIS and D. D. BONNYCASTLE. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 574-578, Nov., 1961. 1 ref.

A new derivative of chloral hydrate, chlorhexadol, was investigated at Seton Hall College of Medicine and Dentistry, Jersey City, to determine whether it retained the desirable hypnotic features without the untoward side-effects of the parent compound. The 71 healthy males taking part were given 750 ml. of water before going to bed together with, in turn, one of 3 treatments: (1) a placebo (lactose); (2) 800 or 1,600 mg. of chlorhexadol; (3) 50 or 100 mg. of quinalbarbitone. On nights when they took the larger dose of chlorhexadol or 50 mg. of quinalbarbitone subjects slept an average of 90 minutes longer than when they had the placebo. The smaller dose of chlorhexadol was ineffective. No undesirable side-effects were observed.

1056. Clinical Trial of Centrophenoxine in Gerlatrics (52 Cases). (Essai clinique de la centrophénoxine en gériatrie (52 cas))

H. Destrem. Presse médicale [Presse méd.] 69, 1999-2001, Oct. 28, 1961. 8 refs.

"Centrophenoxine" (ANP 235; benactyzine) was given orally in doses of 400 to 800 mg. daily to 52 elderly patients in various diagnostic categories. The author claims that 11 patients with confusional states were improved without relapse after 6 to 8 weeks' treatment; 8 cases of Parkinsonism were all improved for indefinite periods with the help of the usual drugs effective against Parkinsonism; similar results were obtained in-cases of prolonged mental confusion in the course of protracted febrile illnesses; 7 out of 12 cases of mental deterioration in the course of hemiplegia were improved; and 5 out of 7 cases of senile disorientation were quickly relieved. Tolerance of the drug was generally excellent. Some patients experienced agitation at the same time as they obtained general and psychological improvement; but this could usually be overcome with sedatives. A few experienced insomnia, and the drug had to be withheld at night. In some cases it had a delayed action, becoming effective only after one to 3 weeks' treatment. The author considers this drug to be of potential value in the treatment of the cerebral syndromes of old people. J. N. Agate

1057. Methotrimeprazine: a New Phenothiazine Derivative with Analgesic Properties

L. LASAGNA and T. J. DEKORNFELD. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 887-890, Dec. 2, 1961. 5 figs., 11 refs.

Methotrimeprazine (levomepromazine), a phenothiazine derivative, has been used for the treatment of psychiatric disorders. It also has analgesic properties, and this paper from Johns Hopkins University School of Medicine, Baltimore, describes a "double-blind" trial in the treatment of postoperative and postpartum pain.

The pain-relieving properties of subcutaneous doses of 5 mg., 10 mg., and 15 mg. of methotrimeprazine maleate were compared with those of doses of 10 mg. of morphine sulphate in 66 patients who had undergone surgery. The mean result was that 10 or 15 mg. of methotrimeprazine was equivalent to 10 mg. of morphine, and 5 mg. of methotrimeprazine was rather less effective. When 25 mg. of methotrimeprazine was given orally to 22 postpartum patients its effect on pain could not be distinguished from that of a placebo. None of the postportup patients admitted to any side-effects, but 4 of the postpartum patients fainted, 4 became drowsy, and one vomited. However, sedation was not thought to be excessive.

The study suggests that methotrimeprazine is worthy of further investigation as an analgesic. The apparently disappointing results in the postpartum cases were not unexpected, since even morphine is disappointing if it is given orally.

T. B. Begg

1058. Chlordiazepoxide as a Broad-spectrum Psychosedative

I. N. ROSENSTEIN and C. W. SILVERBLATT. Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.] 9, 1003-1012, Nov., 1961. 12 refs.

The sedative effect of chlordiazepoxide ("librium.") was tested at the Veterans Administration Hospital, Coral Gables, Florida, on 125 patients [age range not stated] suffering from a variety of disorders, including alcoholism, gastro-intestinal disease, acute myocardial infarction, hypertension, pulmonary disease, carcinoma, and psychoneurosis. Patients were selected on the basis of their need for sedation, muscle relaxation, appetite stimulation, or anticonvulsant therapy, most of them being specifically told that a new drug was being used which had proved of value to others. The dosage was 25 to 100 mg. 3 times daily. Results were assessed on subjective evidence and recorded simply as complete relief, partial relief, or no relief of symptoms.

Of the 75 in-patients treated, it is claimed that 84% obtained either complete or partial relief of anxiety, insomnia, and anorexia; and all but one of the 50 outpatients "responded favourably to the drug". The drug was most effective in angina pectoris, cardiac infarction, and alcoholism, but was of little value when severe pain was present. The only side-effect observed was ataxia. The drug was effective within 2 to 6 hours of administration, and its action continued for 36 to 48 hours after administration ceased. [There were no controls.]

J. N. Agate

Chemotherapy:

Coliston (Coly-mycin) in Resistant Bacterial Infections:
 a Clinical Appraisal

E. M. YOW, E. TAN, L. SHANE, S. SCHONFELD, and H. ABU-NASSAR. Archives of Internal Medicine [Arch. intern. Med.] 108, 664-670, Nov., 1961. 3 figs., 17 refs.

The authors of this paper from Baylor University College of Medicine and Jefferson Davis Hospital, Houston, Texas, report a clinical trial of colistin in a number of antibiotic-resistant bacterial infections. The drug was given intramuscularly to 83 patients (5 with meningitis also received it intrathecally) in a daily dosage ranging from 59 to 133 mg. (average 66 mg.) in adults and 0.5 to 5 mg, per kg, body weight in children. It was particularly successful in patients with infections due to Pseudomonas aeruginosa, which was always sensitive to this antibiotic. In infections due to other organisms sensitivity was very variable, some strains being sensitive and others not; in a few cases concomitant infections interfered with recovery. There were very few undesirable side-effects and the injections were relatively painless, in contrast to injections of the closely related polymixin B.

V. J. Woolley

1060. Antistaphylococcal Activity of Sodium Methicillin 2:6-Dimethoxyphenyl Penicillin: Penicillin X-1497 A. White and D. T. Varga. Archives of Internal Medicine [Arch. intern. Med.] 108, 671-678, Nov., 1961. 10 figs., 19 refs.

The bacteriostatic and bactericidal concentrations of methicillin, benzylpenicillin, phenoxymethylpenicillin, and phenethicillin were determined by a dilution method for various strains of staphylococci isolated from patients at the Louisville General Hospital, Kentucky. Strains of staphylococci producing a penicillinase were highly susceptible to methicillin, but resistant to the other antiblotics; against strains which did not produce penicillinase benzylpenicillin was found to be the most potent antibiotic. A considerable degree of antistaphylococcal activity was present in the serum and transudates of patients receiving methicillin, and signs of penicillin toxicity were slight and transient. It was highly effective in nasal carriers of staphylococci.

V. J. Woolley

1061. Tretamine Compared with Nitrogen Mustard in the Palliation of Inoperable Lung Cancer A. W. Lees. Lancet [Lancet] 2, 900-901, Oct. 21, 1961. 5 refs.

The author, at Ruchill Hospital, Glasgow, compared the effects of tretamine with those of nitrogen mustard in the treatment of inoperable lung cancer. The tretamine was given in a single intravenous dose of 15 to 25 mg. to 18 cases, while 16 other cases received one intravenous dose of 30 to 40 ml. of nitrogen mustard. Of the tretamine-treated cases, 10 obtained symptomatic relief and 7 had some radiological improvement; toxic

side-effects occurred in 14. Of the patients receiving nitrogen mustard therapy, 13 had symptomatic relief and 9 radiological improvement; none had side-effects. Thus tretamine proved less effective and much more dangerous than nitrogen mustard.

G. Calcutt

1062. Chemotherapy of Cancer. [Review Article] T. C. HALL. New England Journal of Medicine [New Engl. J. Med.] 266, 129-134, Jan. 18; 178-185, Jan. 25; 238-245, Feb. 1; and 289-296, Feb. 8, 1962. 32 figs., bibliography.

1063. Thiotepa in the Treatment of Tumours of the Bladder

H. C. JONES and J. SWINNEY. Lancet [Lancet] 2, 615-618, Sept. 16, 1961. 3 refs.

This is a preliminary report of experience at the General Hospital, Newcastle upon Tyne, in the treatment of bladder tumours by direct instillation into the bladder of an alkylating agent triethylene thiophosphoramide (thiotepa). In view of possible damage from systemic absorption the authors estimated the amount of thiotepa which would be absorbed when the drug was retained in the bladder for 3 hours; this was found to be about one-third of the dose instilled.

In the early part of the investigation 30 mg. of thiotepa in 50 ml. of sterile water was instilled into the empty bladder of a moderately dehydrated patient, the dose being gradually increased to 90 mg. In every case 4 doses were given at intervals of 2 to 3 days. Later in the study patients were given 4 doses each of 120 mg. of thiotepa without ill effect. A blood count was carried out at weekly intervals. Of 16 patients treated, 12 had multiple papillary tumours with no evidence of infiltration, one patient had a solitary papillary tumour which was not resectable because of a urethral stricture, and 3 had recurrent infiltrating neoplasms with haematuria.

There was almost complete clearance of the tumours in 8 of the patients with multiple papillary growths, although 2 of them required a further course of treatment and 4 had needed diathermy of residual minute tumours. In 3 patients the response was incomplete and in 2 no effect was observed. Of the 3 patients with haematuria, one was cured, one responded partly, and one showed no change. Complications of treatment were reversible bone-marrow depression in 2 patients and urinary infection, probably as a result of catheterization, in a further 3 patients.

The authors point out the difficulty of determining the optimum dosage in view of the continued dilution of the dose by urine and the effect on the normal bladder wall. They suggest that other anti-tumour agents should be tried but advocate the method they describe in cases of multiple papillary tumours.

J. S. Malpas

Infectious Diseases

1064. Effect of Methicillin Spray on Staphylococcal Colonisation and Lesions in a Nursery

J. C. Ulstrup and A. ØDEGAARD. Lancet [Lancet] 2, 1227-1229, Dec. 2, 1961. 1 fig., 9 refs.

The effect of a methicillin spray on staphylococcal colonization and lesions in infants was investigated in the nursery rooms of two maternity wards on adjacent floors at Aker Hospital, Oslo, each ward measuring approximately 400 c. metres and being similarly arranged. Untreated wards served for purposes of control. After an introductory period of 4 weeks, spraying was carried out for 2 weeks with 4 g. of methicillin daily and for 5 weeks with 2 g. daily. It was found that 6% of the infants' noses were colonized during the period of spraying, compared with 34% during the control period. Observation of the number of infective lesions, however, showed that there was no reduction, the percentage incidence following deliveries during a spraying period, being 20.8 and during control periods 17.6. No effect on colonization was detected in the untreated ward during the period of spraying in the other.

Although it is frequently found that the suppression of Gram-positive organisms may promote the growth of Gram-negative bacteria, *Escherichia coli* was found in only a few instances in the infants in the present investigation. No untoward effects attributable to the spraying were observed in the infants, but 2 nurses, who were previously "skin-healthy", had small, vesiculo-eczematous areas on the forearms at the end of the spraying and complained of general itching. A scarification test was carried out on all the nurses after the end of the investigation, but none of them showed any hypersensitivity to methicillin.

R. G. Meyer

VIRAL DISEASES

1065. Controlled Trial of "Virugon" in Treatment of Measles

E. J. HOPKINS, A. M. PYE, M. SOLOMON, and S. SOLOMON. *British Medical Journal [Brit. med. J.]* 2, 1263–1264, Nov. 11, 1961. 14 refs.

The chief constituent of "virugon", a combination of drugs marketed in Britain as a non-toxic antiviral agent, is N^1 -anhydrobis-(β -hydroxyethyl) biguanide hydrochloride, the "synergists" in the combination being atropine methonitrate and scopolamine methonitrate. Several workers have claimed that it is of value in the prevention of influenza, and there is evidence that it reduces the mortality in young hamsters given intracerebral injections of measles virus.

In an urban general practice in Liverpool the authors carried out a double-blind controlled clinical trial of virugon in the treatment of measles. A group of 19 children with measles were given 100 mg. of virugon 3

times daily while a group of 22 similar children received 100 mg. of a placebo, the tablets being identical; children under 3 years of age received half the dosage. In the majority of the patients the treatment was started on the day of the onset of the rash. No significant differences could be demonstrated between the treated and the control groups in respect of the course of the temperature, duration of the rash and the illness, and the incidence of complications. Virugon was found not to have any value in the treatment of measles.

H. Stanley Banks

1066. Immunization of Preschool Children with Oral Pollovirus Vaccine

D. M. HORSTMANN, J. R. PAUL, M. GODENNE-MCCREA, R. H. GREEN, E. M. OPTON, A. I. HOLTZ, and J. C. NIEDERMAN. *Journal of the American Medical Association [J. Amer. med. Ass.]* 178, 693-701, Nov. 18, 1961. 5 figs., 18 refs.

The authors report from Yale University School of Medicine the results of a study of the most effective and convenient dosage schedule for the Sabin strains of oral poliovirus vaccine, which was carried out in January, 1960, among 348 pre-school children living in 4 lower-income housing estates and an adjacent residential district in New Haven, Connecticut. Of the 195 families approached, 93% agreed to participate. Only children from 6 months to 5 years of age who had received at least one dose of Salk-type vaccine were included; although 79% had received 3 or more doses of killed virus vaccine, only 23% were positive to all 3 virus types, while 22% were triple negative.

Three dosage schedules were compared: (A) Monovalent vaccines of Type 1, Type 3, and Type 2 each given separately in that order one month apart in a dose of 0.2 ml. adjusted to contain 100,000 TCD₅₀ (250,000 TCD₅₀ according to Sabin's laboratory). (B) Monovalent Type-1 vaccine followed 6 weeks later by a bivalent vaccine of Types 2 and 3, the dosage being the same as in Schedule A. (C) A trivalent vaccine given on 2 occasions 6 weeks apart; the dosage of each type in this case being 1,000,000 TCD50. The age, vaccine history, and prevaccination antibody status of the children receiving each schedule were closely comparable. Antibody determinations were carried out on filter paper blood specimens, using the micromethod of Green and Opton with one hour's incubation of the virus-serum mixtures. This method, while being quite as sensitive as the conventional test of inhibition of cytopathic effect, also does not detect antibody of "low avidity" type.

The number of conversions for all 3 virus types was high and closely similar for all 3 schedules, the over-all conversion rates being 95% for Type 1, 98% for Type 2, and 86% for Type 3, the triple negative children responding as well as did those who lacked only one or two antibodies. The acquisition of antibody and the titre

level reached following oral vaccination was not influenced by the number of doses of Salk-type vaccine previously received or by the age of the child. In most instances, the correlation between antibody conversion and excretion of poliovirus was relatively close. After Schedule B the excretion of Type-2 virus was overshadowed by that of Type 3 when they were given together, but this was not the case when the trivalent vaccine was given. The presence of prevaccinal antibody of titre 1:512 and above was an important determinant of viral excretion only in the case of the Type-1 oral vaccine virus. A year after oral vaccination little decline in antibody levels was observed in 63 originally triple negative children.

It is suggested by the authors that these results emphasize the desirability of giving oral vaccine to young pre-school children regardless of their previous poliomyelitis vaccination history. They also indicate that while all the 3 schedules employed gave equally satisfactory results, the larger dosages in Schedule C had no advantage over the smaller doses used in the other 2 schedules.

A. Ackroyd

1067. Inoculation of Human Volunteers with Parainfluenza Virus Type 3

A. Z. KAPIKIAN, R. M. CHANOCK, T. E. REICHELDERFER, T. G. WARD, R. J. HUEBNER, and J. A. BELL. *Journal of the American Medical Association [J. Amer. med. Ass.*] 178, 537–541, Nov. 11, 1961. 2 figs., 14 refs.

This investigation, which was undertaken at the National Institute of Infectious Diseases, Bethesda, Maryland, in an attempt to clarify the role of parainfluenza viruses in infections of adults, was carried out on 28 male volunteer prisoners whose ages ranged from 21 to 56 years.

Antibody titres were determined 12 days before the challenge inoculation. The test group consisted of 17 men, including the 5 with the lowest antibody titres (that is; below 1:64), the other 11 being given a placebo (Hanks saline solution) and serving as controls. A local parainfluenza virus Type 3 was used; it was introduced into the posterior oropharynx by swabbing, spraying, and instillation, an estimated dose of 100,000 TCD₅₀ being administered to each man in the test group. All the subjects were then isolated in individual cells in random order. Investigations included examination of blood samples on the day of inoculation and again 3 weeks later, while throat swabs were also obtained daily for culture.

Only 12 men became infected, none of these being in the control group. Of the subjects with antibody titres of 1:64 or less, 6 out of 7 developed infection, and of those with titres of 1:128 or above, 6 out of 10 developed infection. Clinically, 9 of the 17 in the test group and one of the controls developed an acute respiratory illness. The mean incubation period was 2·2 days and the mean duration of symptoms 5·3 days. The latter were those of a "cold" with nasal discharge and obstruction, sneezing, and coughing. There was erythema of the nasal and pharyngeal mucosa; in no case did the temperature rise above 100° F. (37·8° C.). Chest radio-

graphs, blood counts, and throat swabs showed nothing of significance. Virus was isolated from the throat on the 2nd and 4th days after challenge. It is concluded that in adults para-influenza virus Type 3 is capable of causing acute respiratory disease, but that further investigation is necessary into the various problems of infection.

Kurt Schwarz

HISTOPLASMOSIS

1068. Histoplasmosis Cooperative Study. I. Frequency of Histoplasmosis among Adult Hospitalized Males Veterans Administration Cooperative Study on Histoplasmosis. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 663–668, Nov., 1961. 7 refs.

In order to obtain information regarding the frequency and distribution of histoplasmosis in hospital patients 8 Veterans Administration Hospitals in the Mississippi Valley area and one in Puerto Rico dealing with tuberculosis, other chest diseases, and infectious diseases, were asked to screen all patients on admission for definite signs of mycotic disease. The period of study extended from April 1, 1957, to June 30, 1958, and the tests made included complement fixation, using as antigens Histoplasma capsulatum and Blastomyces dermatitidis (both in the yeast phase), a collodion agglutination test for H. capsulatum (mycelial phase), and sputum cultures for fungi.

Out of a total of 5,756 patients admitted during the period, 639 (11%) were reported to have positive serclogical tests for histoplasmosis, blastomycosis, or coccidioidomycosis and in this paper the records of 625 of these are analysed. Histoplasmosis was confirmed in 51 cases (0.9%), 29 being new cases and 22 already known cases; 5 patients had tuberculosis as well. The histoplasmosis was of the chronic pulmonary type in 45 cases. acute pulmonary in 5, and extrapulmonary in one. Skin tests for histoplasmosis performed in 50 cases gave a positive result in 46 (92%). Of the remaining 474 cases not diagnosed as being histoplasmosis, the skin tests were positive in 211 (52%), that is, similar in proportion to unselected hospital admissions in this endemic area. In 237 the sputum was positive for acid-fast bacilli. In 599 patients a positive serological test was the initial indication for further study. It was shown that serological tests giving a positive titre of 1:32 or more in the yeast-phase complement fixation test showed closer correlation with cases of histoplasmosis than those with positive sputum cultures. High positive titres were seldom found in patients with other diseases and no cross-antigenicity was noted in 8 cases of coccidioidomycosis. Since histoplasmosis is more frequent in some hospitals than others, a systematic survey should be of interest especially in verifying clinically active cases. When serological tests are to be used the first specimen of serum should be taken before performing the skin tests, since the latter stimulate antibody production. In the presence of pulmonary disease, concomitant tuberculosis should I. M. Librach . also be excluded.

Tuberculosis

1069. BCG Vaccination in Tuberculous Households S. R. ROSENTHAL, E. LOEWINSOHN, M. L. GRAHAM, D. LIVERIGHT, M. G. THORNE, and V. JOHNSON. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 690-704, Nov., 1961. 20 refs.

The authors describe from the University of Illinois, Chicago, a strictly controlled study of B.C.G. vaccination of newborn infants in tuberculous households during the years 1941 to 1960. The multiple puncture technique was used and all 451 infants in the study, including the 231 who were vaccinated and the 220 junvaccinated controls, were isolated at or soon after british in foster homes. The two groups were shown to be comparable in respect of home and environmental contact with tuberculosis, sex, race, birth weight, followup care, and subsequent diseases.

Among the 231 vaccinated infants there were 3 cases of tuberculosis (0.68 per 1,000 per year), and among the 220 not vaccinated 11 cases (2.63 per 1,000 per-year); that is, the vaccinated showed a reduction in the over-all incidence of tuberculosis of 74%, a statistically significant difference (P=0.043). Of the 11 cases of the disease among the controls, 7 (1.67 per 1.000 per year): were not fatal, while the 4 deaths from tuberculosis in this group represented a rate of 0.96 per 1,000 per year. No case of tuberculous meningitis or miliary tuberculosis occurred in the vaccinated group, but there were 4 such cases among the controls; this difference, however, was not found to have statistical significance (P>0.10). A tuberculin conversion rate of 99.6% was obtained in the vaccinated group. [Those interested in this problem should read the paper in full.] W. Raymond Parkes

RESPIRATORY TUBERCULOSIS

1070. The Role of Diet in the Treatment of Pulmonary Tuberculosis: an Evaluation in a Controlled Chemotherapy Study in Home and Sanatorium Patients in South India C. V. RAMAKRISHNAN, K. RAJENDRAN, P. G. JACOB, W. Fox, and S. RADHAKRISHNA. Bulletin of the World Health Organization [Bull. Wld Hlth Org.] 25, 339-359, 1961. 1 fig., 16 refs.

A study was undertaken [at the Tuberculosis Chemotherapy Centre, Madras] of the diet of 157 patients with pulmonary tuberculosis admitted to a controlled comparison of treatment with isoniazid plus PAS for a year at home with the same treatment in sanatorium. The patients were drawn from a poverty-stricken section of the community living in overcrowded conditions in Madras City. A comparison has been made of the dietary status of the home and the sanatorium patients before and during treatment, and the role of the diet in the attainment of bacteriological quiescence of the tuberculous disease has been evaluated. The assessments of the dietary intake were made by the oral questionnaire

method. In an analysis based on 45 patients it gave results similar to a dietary weighment technique.

The dietary intake before the start of treatment was assessed for all the 157 patients, and 112 of them had another assessment in the second 6 months of treatment; the remaining 45 patients were investigated at five setdates during treatment—namely, at 6 weeks, 3 months, 6 months, 9 months and one year. Before treatment the patients in both series had poor and similar diets. During the early months of treatment, the dietary intake of the patients in both series increased. However, the sanatorium patients received a clearly superior diet throughout the year in terms of total calories, fats, total and animal proteins, phosphorus and several of the vitamins. The home patients were physically more active during treatment than the sanatorium patients, further accentuating the dietary disadvantage of the home series.

The home patients gained on the average 10.8 lb. [4.9 kg.] in weight over the 12-month period, as compared with 19.8 lb. [8.9 kg.] for the sanatorium patients. This greater weight gain among the sanatorium patients was not, however, indicative of superior clinical results. The response to treatment (as measured by the radiographic and bacteriological progress) was not directly associated with the level of dietary intake of any of the food factors, either in the patients treated at home or in those treated in sanatorium.

It may be concluded that none of the dietary factors studied appears to have influenced the attainment of quiescent disease among tuberculous patients treated with an effective combination of antimicrobial drugs for a period of one year. The successful initial treatment of patients at home is therefore possible even if the levels of dietary intake are low.—[Authors' summary.]

1071. Prevalence and Early Attack Rate of Tuberculosis among Close Family Contacts of Tuberculous Patients in South India under Domiciliary Treatment with Isoniazid plus PAS or Isoniazid Alone

C. V. RAMAKRISHNAN, R. H. ANDREWS, S. DEVADATTA, W. FOX, S. RADHAKRISHNA, P. R. SOMASUNDARAM, and S. Velu. Bulletin of the World Health Organization [Bull. Wld Hlth Org.] 25, 361–407, 1961. 9 figs., 17 refs.

The authors present a report from the Tuberculosis Chemotherapy Centre, Madras, on the prevalence and attack rate of tuberculosis among close family contacts of tuberculous patients in South India undergoing domiciliary chemotherapy either with isoniazid plus PAS or with one of three regimens of isoniazid alone. The report gives (a) the prevalence of tuberculosis among the contacts at the time of diagnosis of the disease in the patients and (b) the incidence of tuberculosis in the contacts during the first years of treatment of the patients. The contacts were divided into four series, corresponding to the four chemotherapeutic regimens of the patients.

The prevalence of active tuberculosis was found to be particularly high among children under 5 years of age, being 12% as compared with 7.6% for all age-groups combined. The incidence of active tuberculosis during the year of treatment of the patients was also found to be highest in the under 5-years' age-group—a further indication that child contacts are especially vulnerable to infection. The incidence was considerably higher in the first quarter of the year than in the other quarters, and it was lowest in the last quarter. This finding, together with the fact that the attack rates in the four contact series were not related either to the duration of bacteriological positivity in the patients or to the period of excretion of isoniazid-resistant organisms by the patients, suggests that the major risk to contacts in the first year results from exposure to the patient before treatment rather than from exposure during treatment. These results thus confirm the findings in an earlier study by the Centre of the contacts of patients in a controlled comparison of chemotherapy with isoniazid plus PAS at home and in sanatorium.—[Editorial summary.]

1072. Progress in the Second Year of Patients with Quiescent Pulmonary Tuberculosis after a Year of Domiclliary Chemotherapy, and Influence of Further Chemotherapy on the Relapse Rate

S. Velu, R. H. Andrews, J. H. Angel, S. Devadatta, W. Fox, P. R. J. Gangadharam, A. S. L. Narayana, C. V. Ramakrishnan, J. B. Selkon, and P. R. Somasundaram. *Bulletin of the World Health Organization* [Bull. Wld Hlth Org.] 25, 409–429, 1961. 23 refs.

This study from the Tuberculosis Chemotherapy Centre, Madras, summarizes the progress during the second year of those patients in a 1-year comparison of four domiciliary chemotherapeutic regimens (isoniazid plus PAS and three regimens of isoniazid alone) whose pulmonary tuberculosis had attained bacteriological quiescence at the end of the year of chemotherapy. During the second year, about half of the patients received further chemotherapy, with isoniazid alone, and the remainder received a placebo, calcium gluconate. The main objects of the study were to determine the influence on the progress during the second year of (a) a second year of chemotherapy with isoniazid alone, (b) residual cavitation at the end of the first year, and (c) the chemotherapeutic regimen received during the first year, and to compare the results with those obtained in an earlier study by the Centre of the progress during. the second year of patients with quiescent pulmonary tuberculosis after a year's chemotherapy with isoniazid plus PAS at home or in sanatorium.

The results of the present study, which was planned on the same lines as the earlier one, showed that relapse in the second year was unrelated to the chemotherapeutic regimen received in the first year, and it was therefore permissible to amalgamate the findings in the two studies. The amalgamated results showed that the relapse rate in the second year was low (5.9%) and that a second year of treatment with isoniazid alone was of definite value for the patients with no residual cavitation at the end of the first year, but had no effect on the relapse rate

of those, with residual cavitation. The combined data from the two studies have thus clarified the position with regard to the effectiveness of isoniazid in preventing bacteriological relapse in patients without residual cavitation, slight evidence of which was apparent in the earlier study.—[Editorial summary.]

1073. Triamcinolone in Primary Pulmonary Tuberculosis: a Controlled Trial

S. E. KEIDAN and R. McL. TODD. Lancet [Lancet] 2, 1224-1227, Dec. 2, 1961. 4 figs., 6 refs.

This investigation, reported from Alder Hey Children's Hospital, Liverpool, was designed to compare the effects of chemotherapy combined with corticosteroid therapy with those of chemotherapy alone in recent primary pulmonary tuberculosis in children. The 16 children taking part-all received a course of chemotherapy: streptomycin intramuscularly in a daily dose of 20 mg. per lb. (44 mg. per kg.) body weight with isoniazid 5 mg. per lb. (11 mg. per kg.) body weight daily for 12 weeks. In addition, alternate children were given triamcinolone orally, 0.25 mg. per lb. (0.55 mg. per kg.) body weight daily for 4 weeks, and then 0.125 mg. per lb. (0.275 mg. per kg.) body weight daily for 4 weeks, gradually reducing the dose and stopping after a further 2 weeks. Patients treated with corticosteroids showed definite and sometimes striking radiological improvement within a month when compared with the controls, who did not show any appréciable change even within 3 months. The authors consider-that corticosteroids suppress the allergic response to tuberculin, as shown by the reversal of the Mantoux reaction in 5 of the 8 patients, and also reduce the size of the lymph nodes, relieving pressure on the bronchi. They recognize the possible danger of this therapy in patients infected with drug-resistant organisms.

I. Ansell

1074. The Streptomycin Concentration in Tuberculous Cavities

K. D. Arosenius, V. O. Björk, and G. Laurell. *Thorax* [*Thorax*] 16, 361-363, Dec., 1961. 2 refs.

The authors of this paper from the University Hospital. Uppsala, Sweden, state that since they did not find it possible to use radioactive isotopes added to the streptomycin molecule to determine whether streptomycin was present in tuberculous cavities, they chose a biological test of streptomycin concentration which depended on the arrest of growth of different bacteria of known resistance. A significant concentration of streptomycin was found in 8 out of 9 thin-walled cavities and in 7 out of 13 thick-walled cavities; there was no demonstrable concentration of streptomycin in a tuberculoma. The concentration in the tuberculous lung tissue varied between 0.01 and 1.0 μ per ml. The total dose of streptomycin given before the operation did not appear to influence the concentration in the specimen. However, when streptomycin was given in a dosage of 1 g. daily a therapeutic concentration was found within the specimen in 10 cases out of 12, whereas when 1 g. was given every other day, with the last dose on the day before the operation, streptomycin could be demonstrated in 7

specimens out of 12. The authors conclude that administration of streptomycin is effective within thinwalled cavities but within thick-walled cavities the concentration of streptomycin is not high and in 2 cases of tuberculoma there was no demonstrable concentration of the drug. They therefore advocate active surgical treatment with resection in cases of thick-walled cavities and of tuberculomata after a short period of preoperative treatment with streptomycin. *Kenneth M. A. Perry*

1075. The Treatment of Chronic Cavitating Pulmonary Tuberculosis by Long-term Chemotherapy D. H. BLAKE. Tubercle [Tubercle (Lond.)] 42, 438-443, 1961. 3 refs.

Long-term chemotherapy was given at Markfield Hospital, Leicester, to 50 patients with chronic cavitating pulmonary tuberculosis not amenable to surgery and sputum cultures sensitive to at least two of the three standard antituberculous drugs. Of the 50 patients, 22 had had chemotherapy previously and they progressed almost as well as the 28 who had not. Initial sputum conversion was achieved in 46 patients. Of 45 followed up for 3 years, 40 were sputum negative and of 24 followed up for 5 years, 22 were sputum negative.

The results appeared to indicate that patients given a treatment regimen containing streptomycin did better than those who did not receive this drug. However, in 7 of the 29 patients receiving streptomycin vertigo developed. In 6 patients there was further drug resistance during treatment.

G. M. Little

1076. Tuberculosis and Cardiopulmonary Failure L. Levinsky. Diseases of the Chest [Dis. Chest] 40, 564-571, Nov., 1961. 4 figs., 16 refs.

The author discusses the incidence and diagnosis of cardio-pulmonary failure among 6,854 patients with pulmonary tuberculosis seen at the University Clinic for Tuberculosis, Prague, between 1946 and 1957. Associated with the use of antituberculous drugs there was an increase in the average duration of the disease from 2.8 to 7.5 years owing to an increase in the development of chronic forms. Similarly, the average age in fatal cases had gone up from 37 to 57.5 years, and 75% of patients who died suffered from the chronic form of the disease with cavitation. In addition, there was an increase inthe number of cases with "open healed cavities" from 0.2% in a series reported before the chemotherapeutic era to 10% in the present series. Cor pulmonale was found as the cause of death with increasing frequency, reaching 23% during the last 4 years of the survey. The post-mortem changes of cor pulmonale-namely, hypertrophy or dilatation of the right ventricle with venous congestion of the liver-are compared with the clinical findings, such as cyanosis, raised resting pulse rate, signs of congestive cardiac failure, radiologically demonstrated enlargement of the heart, cranial displacement of thepulmonary hilus, and dilatation of the main branches of the pulmonary artery. In two-thirds of the cases where signs of chronic pulmonary hypertension were found at necropsy this had not been suspected during life. The author lists a number of signs which should suggest compensated chronic cor pulmonale; these include a palpable accentuated or split second sound over the pulmonary area and a pulmonary diastolic murmur.

H. F. Reichenfeld

1077. Pulmonary Tuberculosis in Old Age J. Adler, G. Librach, and M. Berlin. Diseases of the Chest [Dis. Chest] 40, 504-512, Nov., 1961. 7 refs.

The authors report their experience with 197 elderly tuberculous patients at the Home for Tuberculous Aged, Pardessia, Israel, between 1953 and 1958. The institution consists of a number of small buildings with accommodation for married couples to live together, has radiological and bacteriological facilities, an occupational therapy unit, and a day centre. There were 138 males and 59 females in the series, and in addition 41 healthy spouses who had joined their husbands or wives; 151 of the patients were over 65 years of age, including 83 between 70 and 79 years and 14 over 80. At the time of admission there were 132 patients whose condition was regarded as "unstable", including 110 with a positive sputum. A liberal regimen in respect of rest prevailed at the home, both in view of psychological considerations and to prevent the cardiovascular complications of prolonged rest in bed.

During the 6 years 131 patients received treatment with antituberculous drugs, either continuously or intermittently. By the end of the period 64 patients had died, but in only 25 instances was the cause of death directly related to the tuberculous process. Of the remainder, 40 had been discharged, 32 transferred to hospital, and 93 were still at Pardessia. During their stay 30 patients had shown some deterioration in their tuberculous state, 62 had remained stationary, and 105 had improved. Of the 110 patients who entered the home with positive sputum, conversion was obtained in 38. None of the spouses became infected, in spite of the close contact and the fact that 4 of them suffered from diabetes mellitus.

H. F. Reichenfeld

1078. Pulmonary Tuberculosis in Contacts: a Ten Year Survey

A. W. LEES, G. W. ALLAN, J. SMITH, and W. F. TYRRELL. Diseases of the Chest [Dis. Chest] 40, 516-521, Nov., 1961. 4 refs.

The incidence of tuberculosis in 664 household contacts of 155 people discovered to have active pulmonary tuberculosis in 1948 [in Glasgow] was investigated. Over a 10-year period 81 (12%) of the 664 contacts developed active tuberculosis; 8 (1.2%) non-respiratory tuberculosis, 12 (1.8%) childhood-type primary pulmonary tuberculosis necessitating hospital treatment, and 61-(9.2%) adult-type pulmonary tuberculosis. Of the 61 cases of adult pulmonary tuberculosis, about one-third (22) were discovered in the first year, about one-half (32) in the first 2 years, and about three-quarters (46) in the first 5 years. In women contacts aged less than 25 years in 1948, all the disease detected was found in the first 5 years, but in men contacts and in women contacts aged 25 to 44 years in 1948, disease continued to appear throughout the 10-year period. Of 79 women contacts

aged more than 44 years in 1948, none developed disease. These findings suggest that women contacts aged less than 25 years should be supervised for 5 years, that women contacts aged more than 44 years need no supervision beyond an initial x-ray film, and that other classes of contacts should be supervised for 10 years at least. Long-term supervision still presents many practical difficulties, and at best can only limit and not prevent dissemination of infection. Chemoprophylaxis for contacts also presents difficulties, but it is suggested that its potential advantages seem so great that a trial is indicated.—[Authors' summary.]

TUBERCULOUS MENINGITIS -

1079. Role of Intrathecal Hydrocortisone in Tuberculous Meningitis in Children

S. P. KHATUA. British Medical Journal [Brit. med. J.] 2, 1597-1599, Dec. 16, 1961. 13 refs.

At the paediatric clinic of the Calcutta Medical College 43 children suffering from tuberculous meningitis were studied between July, 1959, and June, 1961. In half of these patients tubercle bacilli were recovered from the cerebrospinal fluid (C.S.F.). All had moderately or advanced disease and all received the same antituberculous chemotherapy (streptomycin, isoniazid, and PAS), but none were given antibiotics intrathecally. Alternate patients (20) were given prednisolone orally in a daily dose of 10 to 20 mg. daily for 3 weeks, while the remaining 23 were given intrathecal hydrocortisone in a dosage of 12.5 to 25 mg. daily for 6 days and then on alternate days for a further 6 injections. The C.S.F. was examined in both groups on 4 occasions between admission and discharge. In the oral steroid group 8 of the 20 patients (40%) survived and in the intrathecal group 14 out of 23 (61%) survived. The C.S.F. changes tended to return towards normal more quickly in the intrathecal group. The infrequency of the examination of the C.S.F. makes this observation only a little less significant.]

Most of the patients were unconscious for a long time, but in the intrathecal group this state lasted for only 2 to 12 days as compared with 22 to 60 days in the oral steroid group. Also, 4 of the 8 survivors in the oral group had severe neurological sequelae as compared with only 2 of 14 in the intrathecal group. [The survival rates in both groups were below optimum; they could have been improved by intrathecal administration of streptomycin or isoniazid. The "final," survival figures relate to a very short period of observation.]

Jolin Lorber

1080. The Prognosis of Tuberculous Meningitis in the Isoniazid Era

W. Weiss and H. F. FLIPPIN. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 423-430, Oct., 1961. 1 fig., 6 refs.

At the Philadelphia General Hospital tuberculous meningitis was diagnosed in 73 patients during the period 1952-7 inclusive. They were all treated with isoniazid and all but one with streptomycin as well [but otherwise

there was no uniform or planned method of treatment]. Tubercle bacilli were recovered from the cerebrospinal fluid in [only] 56% of cases, though "evidence of tuberculosis was obtained in 89% of those who died and 71% of those who survived". Intrathecal streptomycin was given to 12 patients (all children), all during 1952-4, and 11 of these survived.

Altogether 13 (76%) of 17 children (0 to 10 years) survived compared with 18 (56%) of 32 young adults and 4 (17%) of 24 patients over 40. It is concluded that intrathecal treatment is unnecessary, [in the face of apparently strong evidence that those patients who had intrathecal treatment fared far better than those who did not]. It is also considered that sequelae were commoner in those who had intrathecal treatment. [But were these patients selected because they had more severe disease?] Among the prognostic factors listed the authors found no correlation between the state of consciousness on admission and the ultimate outcome [contrary to virtually all other published reports.] In 12 cases systemic steroid treatment was also given, without convincing the authors of its value; 7 of these 12 patients died.

[This is a poorly documented and sometimes self-contradictory paper. The results are poor by current standards. If one reads between the lines a good case is made out for intrathecal treatment, yet the authors attempt to convince themselves of the opposite.]

John Lorber

1081. Long-term Follow-up of 100 Children who Recovered from Tuberculous Meningitis

J. LORBER. Pediatrics [Pediatrics] 28, 778-791, Nov., 1961. 2 figs., 16 refs.

During the 9-year period 1947 to 1955, a total of 170 children suffering from tuberculous meningitis were treated in the Department of Child Health, University of Sheffield, 100 surviving for at least 5 years. These survivors have been assessed in respect of intelligence, educational attainments, character and behaviour, neurological and physical defects, and electroencephalographic (EEG) findings.

The average I.Q. of these 100 children was lower than that of the general population, but the parents of these children belonged largely to the lower social classes. There was a close correlation between the I.Q. and educational progress; most of the children attended a secondary modern school and only 7 attended a grammar school. No change in character or behaviour followed the illness in 88 children. Hearing was normal in 84 of 94 children in whom this was assessed, 6 were partially deaf, and 4 completely deaf. There were 3 totally blind children. Convulsions persisted in 8 children and paralyses were present in 12. Sexual precocity developed in 3 girls and ectopic ossification of the iliopsoas tendons in 3 patients (2 boys and one girl).

The EEG records were normal in 56 out of 97 patients; the commonest abnormality, which was found in 28 patients, was generalized dysrhythmia. An abnormal EEG pattern was observed in 23% of patients who at no time had grossly abnormal neurological signs and in 79% of those patients with obvious neurological lesions.

R. M. Todd

Venereal Diseases

1082. Nongonococcal Urethritis: Topical Treatment with Nitrofurazone

M. D. EVANS. Journal of Urology [J. Urol. (Baltimore)] 86, 409-411, Oct., 1961. 6 refs.

Three groups of patients with non-gonococcal urethritis received urethral suppositories containing nitrofurazone as the basic ingredient with the addition, respectively, of topical anaesthetic, of topical anaesthetic and oestrogen, and of topical anaesthetic and hydrocortisone. The actiology of the urethritis was varied, and some patients had a urethral stricture and others pelvic inflammatory disease as well. There was an unspecified number of women amongst the 54 patients treated. One suppository was inserted daily until symptomatic relief was obtained.

The results were considered to be "excellent" or "good" in most of the cases. The nitrofurazone-anaesthetic combination is said to have been particularly effective in female urethritis and male urethral stricture, while the nitrofurazone-anaesthetic-oestrogen suppository was beneficial in senile and postmenopausal urethritis, and the nitrofurazone-anaesthetic-steroid combination in severe and post-instrumental urethritis.

G. W. Csonka

SYPHILIS

1083. The Diagnostic Problem of Cardiovascular Syphilis. (Il problema diagnostico della sifilide cardiovascolare)

R. VACCARI and E. MANZINI. Minerva medica [Minerva med. (Torino)] 52, 3843-3849, Nov. 7, 1961. 3 figs., 30 refs.

The diagnosis of cardiovascular syphilis presents many difficulties and finally rests on a combination of clinical and radiological signs and the results of laboratory tests.

The present report from the University of Modena is based on a study of 25 cases of cardio-aortic involvement, 13 of the patients having aortitis, 4 aortic regurgitation, 7 an aortic aneurysm, and one a cardiac infarct. The methods of clinical and radiological investigation in these cases are enumerated, but the authors' main concern was with the immuno-allergic reactions.

The mean age of the patients was 54, ranging from 36 to 80 years. In only 9 cases was there a known antecedent syphilitic infection and these patients had had only incomplete courses of treatment, the onset of cardio-vascular syphilis being 13 to 38 years after the primary infection. In 20 patients (80%) some at least of the classic serological reactions were positive, but even when these were negative the treponemal immobilization (T.P.I.) test gave a positive result. On all patients the "luotest", an intradermal test with purified specific antigen prepared from a Nichols strain treponeme from

early rabbit orchitis, was carried out. (The preparation of this antigen is referred to and the test is also discussed with reference to the literature. It is considered to be absolutely specific and to characterize the late stage of syphilis.) This test, as well as the T.P.I. test, gave positive results in all 25 cases.

In addition to the above 25 cases, 2 cases are described in greater detail. They both gave a positive history of syphilis with some treatment, but all serological reactions, including the T.P.I. reaction, were negative, although the response to the luotest was positive. The authors consider that cardiovascular disease with a negative T.P.I. reaction is not of specific origin.

F. Hillman

1084. Treatment of Early Syphilis with Erythromycin A. B. Greaves. *Public Health Reports [Publ. Hith Rep. (Wash.)*] 76, 929-932, Oct., 1961. 12 refs.

As part of a programme being carried out by the District of Columbia Department of Health to seek alternative therapeutic agents to penicillin in the treatment of early syphilis, an assessment was made of the results in 29 patients with early syphilis (primary or early secondary stages), all with dark-field positive tests, who were given orally a total dose of 10 g. of propionyl erythromycin—2 g. initially at the clinic, then 1 g. per day for 6 days, and a final 2 g. at the clinic on the 8th day. Evaluation was made on the basis of clinical examination, dark-field examination (1 week), and the usual serological tests, which were performed at monthly intervals up to one year.

Of the 29 patients only 17 completed treatment and follow-up satisfactorily with a negative serology and normal cerebrospinal fluid findings; of the other 12, 5 were lost to follow-up, 3 failed to respond to therapy, and 4 patients developed reinfections. The 3 failures were all in patients with syphilis in the secondary stage; these showed an initial response, but relapsed in 3 to 4 months. In all cases the dark-field examination became negative within 4 days. At least half the patients suffered gastrointestinal side-effects from the therapy. It is concluded that at these dosage schedules the results obtained with erythromycin are obviously not comparable to those obtained with the usual course of penicillin.

Allene Scott

1085. Rapid Reagin Test with Unheated Serum and New Improved Antigen Suspension

J. PORTNOY, H. N. BOSSAK, V. H. FALCONE, and A. HARRIS. Public Health Reports [Publ. Hlth Rep. (Wash.)] 76, 933-935, Oct., 1961. 8 refs.

In view of the success of the rapid plasma reagin (R.P.R.) test for syphilis as a quick and economical procedure for screening large numbers of patients, search has been made at the Venereal Disease Research Laboratory, Atlanta, Georgia, for a test capable of utilizing

satisfactorily the same antigenic suspension with unheated plasma or unheated serum. The following technique was devised: 0.05 ml. of unheated serum is mixed with 1/45 ml. of improved (Portnoy) R.P.R. antigen suspension on a 14-mm. paraffin-ringed slide and the reaction noted. This test gave 97-4% agreement with the V.D.R.L. test and other standard tests for syphilis in one series of 492 patients and a second group of 100,000 cases examined in New York. The similarity in procedure to the standard V.D.R.L. test will, it is suggested, make this new test a simple one to introduce into the laboratory.

Allene Scott

1086. Sensitivity to the Zone Phenomenon of Syphilitic. "Reagin" Elaborated in Long-standing Syphilis. (Sensibilité au phénomène de zone de la "réagine" syphilitique élaborée au cours de la syphilis ancienne)

R. PAUTRIZEL, F. SZERSNOVICZ, and M. TOULZA. Annales de biologie clinique [Ann. Biol. clin.] 19, 707-714, Oct.-Dec., 1961. 2 figs., 3 refs.

The prozone phenomenon in flocculation tests for syphilis has been attributed to inhibition of the union of antibody with antigen by an excess of antibody, the reaction becoming more intense as the serum is diluted with saline in a quantitative test. In this study the authors, working at the Faculty of Medicine, Bordeaux, have analysed the results obtained over a 6-year period during which, of 90,106 sera examined by the standard Kline test, using a cardiolipin antigen, 21,467 gave positive results, and of these 259 (1.2%) showed zoning reactions. Most of the sera showing zones came from patients with infections of long standing, 149 having tertiary lesions, 101 latent disease, and 9 secondary lesions. Although many sera from cases of early syphilis were examined during the period reviewed, none gave zoning reactions. In 7 of these sera the reaction with undiluted serum was completely inhibited, whereas on dilution titres of 1:8 to 1:256 were obtained. In 243 of the sera there was only partial inhibition of the reaction with undiluted serum, and these gave titres of 1:4 to 1:2,048 on dilution. Nine sera showed a "double zone" effect; thus at first the reaction with undiluted serum was almost maximum. but as dilution proceeded it became first weaker and then stronger again, before finally becoming negative.

The authors suggest that the titre of a serum is not the only factor responsible for the zone phenomenon; zoning occurred most frequently in sera giving titres of 1:32 or 1:64, but 10 of the sera had low titres of 1:8 or less. The total inhibition of low titred sera was most marked with sera from patients with tertiary syphilis, suggesting that the reagin produced at this stage of the disease may be less avid in its reaction with antigen. The sera of some patients may continue to give zoning reactions for long periods; one case is cited in which zoning was seen in 15 separate specimens of serum. The zone effect can be overcome to some extent by enhancing the contact of antibody with antigen by centrifuging the serum-antigen mixture or by increasing the salt concentration used in the Kline test. The authors found zone reactions to be more marked in the Kahn and Meinicke tests, but not to occur at all in the Kolmer

complement fixation test. They recommend that both a complement fixation test and a flocculation test should be used as screening procedures and that when the result of the former is positive but the latter negative, the flocculation test should be repeated by a quantitative technique in order to avoid a false negative result due to a zoning reaction.

A. E. Wilkinson

1087. Studies on Non-specificity Factors in Immunofinorescence Reactions. Importance in the Investigation of Antibodies against the Treponeme of Syphilis. (Étude des facteurs de non-spécificité des réactions d'immunofluorescence. Intérêt dans la recherche des anticorps contre le tréponème de la syphilis)

J. THIVOLET and D. CHERBY-GROSPIRON. Annales de l'Institut Pasteur [Ann. Inst. Pasteur] 101, 869-875, Dec., 1961. 6 refs.

In performing the fluorescent treponemal antibody test the sera are usually diluted 1 in 200 with buffered saline because it has been found that some sera from non-syphilitic patients may give non-specific fluorescence with treponemes at lower dilutions. This necessity for dilution reduces the sensitivity of the test. Working at the Faculty of Medicine, Lyons, the authors have investigated the cause of this non-specific fluorescence.

They found that absorption of the anti-human globulin conjugates used in the test with dried organ powders (mouse and rabbit liver or rabbit testicle) failed to abolish non-specific fluorescence. A conjugate was then prepared from the serum of a patient in whom syphilis could be excluded with certainty, but which nevertheless gave a marked non-specific reaction. This conjugate also showed non-specific staining, leading the authors to conclude that this was a property of the serum itself and not of the conjugates used in the test. Absorption of this conjugated normal serum, or of other normal sera, with powdered rabbit testis was found to abolish non-specific staining, whereas absorption with rabbit liver powder was not so effective. It is thought that substances in the tissue fluids of the testes from which the treponemes have been extracted may react with some normal sera; these substances presumably coat the surface of the treponemes during fixation of the suspension on the slide.

The factors in normal sera responsible for non-specific staining are rendered inactive by heating the sera to 62° C. for 30 minutes, specific antitreponemal antibodies being unaffected by this temperature. The authors recommend that the test should be performed with serum diluted to 1:30 which is then shaken with dried rabbit testis powder for two periods each of one hour, centrifuged, and the supernatant fluid heated to 62° C. for 30 minutes. This procedure has been used to test a hundred normal sera and is thought to give specific results.

A. E. Wilkinson

1088. Involvement of the Aortic Valve and Ascending Aorta in Congenital Syphilis: a Review

F. S. BONUGLI. British Journal of Venereal Diseases [Brit. J. vener. Dis.] 37, 257-267, Dec., 1961 [received Feb., 1962]. 3 figs., 38 refs.

Tropical Medicine

INFECTIOUS DISEASES

1089. An Experiment in the Prevention of Meningococcal Meningitis in Nigeria

R. L. Vollum and P. W. W. Griffiths. Journal of Clinical Pathology [J. clin. Path.] 15, 50-53, Jan., 1962. 1 ref.

Epidemics of meningococcal meningitis recur periodically during the dry season in northern Nigeria and in other parts of Africa having a similar climate. The authors of this paper from the Radcliffe Infirmary, Oxford, describe an experiment carried out in the Danja district of the Katsina province of Northern Nigeria in which 99% of the population of approximately 100,000 received sulphadimidine snuff during the course of one such epidemic. The maximum dose of the snuff was 1 g. and it was planned to give each individual four such doses over a period of 2 days. In fact 87% of the population received four doses and 94% received three doses.

The results were considered to be good. In the 4 weeks before the experiment there were 287 cases of meningitis and in the 4 weeks afterwards there were only 77, including 50 in which no snuff was taken. It is suggested that similar results might be obtained with sulphonamides given by mouth but the dosage required would be much higher.

R. R. Willcox

1090. The Clinical Syndrome of Amebic Abscess of the Left Lobe of the Liver

W. J. Alkan, B. Kalmi, and M. Kalderon. Annals of Internal Medicine [Ann. intern. Med.] 55, 800-813, Nov., 1961. 5 figs., 25 refs.

From Asaf Harofe Hospital, Zrifin, Israel, the authors present 8 cases of the relatively rare condition of amoebic abscess of the left lobe of the liver occurring in 6 males and 2 females, of whom 3 came to necropsy. The major clinical findings included pyrexia in all cases, enlargement of liver in 7, an increased erythrocyte sedimentation rate in 7, a short Weltmann coagulation band in 5, leucocytosis in 7, positive x-ray findings in 6, and good response to anti-amoebic therapy in 4 and partial response in 2. So-called "minor" findings were jaundice in 3 cases, cough in 3, physical changes in the left chest in 3, vomiting in 3, rigor in 2, bloody diarrhoea in 2, Entamoeba histolytica in the stools of 2, and enlargement of the area of cardiac dullness in one case.

The authors state that an enlarged liver, particularly in its left aspect, in a febrile patient with severe pain in the epigastrium or left hypochondrium, or both, is a characteristic finding. On x-ray examination changes in the contour and position of the stomach and pressure on the colon are also characteristic. Left lobe abscesses have a particular tendency to perforate into neighbouring abdominal structures, but extension into the pericardial

sac has also been observed. Jaundice may be comparatively frequent when perforation into the lesser sac has occurred, and it is then obstructive in nature. Although some acute or early cases respond to medical treatment, the authors are of the opinion that an amoebic abscess of the left lobe of the liver which has not responded to conservative treatment within one or 2 weeks constitutes an "almost absolute indication for additional surgical intervention".

R. R. Willcox

1091. Favourable Influence of Testosterone on the Intestinal Sequelae of Amoebiasis. (Influence favorable de la testostérone sur les séquelles intestinales post-amibiennes) L. ESPINOZA. Bulletin de la Société de pathologie exotique et de ses filiales [Bull: Soc. Path. exot.] 54, 703-706, July-Aug. [received Dec.], 1961. 5 refs.

This study was carried out at Guayaquil Hospital, Ecuador, on 23 male patients in whom diagnosis of intestinal amoebiasis was confirmed by stool examination or by sigmoidoscopy. Various forms of the usual specific treatment were given until the protozoon had been eliminated. In spite of cure of the disease, however, 16 of the patients remained ill, with hypochromic anaemia, a raised erythrocyte sedimentation rate, hypoproteinaemia, and abnormal results in liver function tests. On sigmoidoscopy the intestinal membrane was seen to be inflamed. Treatment with vitamins, a high-protein diet, wholeblood transfusions, and intestinal antispastic drugs improved the general condition, but not the intestinal lesions. Finally injections of testosterone proved satisfactory in improving the intestinal condition in all cases over the course of 4 to 6 months. At first the androgen was given in the oily form in a dosage of 50 mg/weekly, but owing to side-effects this regimen was changed to 100 mg. twice monthly of a crystalline preparation. The patients remained in hospital for 4 months.

W. H. Horner Andrews

1092. Immunity in Kala-azar

P. E. C. MANSON-BAHR. Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy Soc. trop. Med. Hyg.] 55, 550-555, Nov., 1961. 6 refs

During recent years kala-azar has become epidemic in the Sudan and Kenya. In this paper from King George VI Hospital, Nairobi, the author first describes the leishmanin (Montenegro) skin reaction, which he has used to survey an area in Kenya where kala-azar is endemic and in another area which is free from the disease. It was found that 15·1% of 1,746 persons tested gave a positive reaction in the endemic area, whereas only 1·5% of 182 persons gave a positive result in the area free from kala-azar:

The author concludes that a positive leishmanin test rate of over 5% shows that kala-azar is endemic in the area. Studies of cross-immunity on a patient cured

of kala-azar showed that he was susceptible to *Leishmania tropica*, but was resistant to East African, Mediterranean, and Indian strains of *L. donovani*.

The author also observed that the ground-squirrel strain of L. donovani was dermatotrophic and produced a skin nodule after the inoculation of culture flagellates, but there was no visceral involvement. In volunteers subjected to this procedure it was shown that 6 to 8 weeks after inoculation the leishmanin test was positive and there was complete immunity to subsequent challenge with kala-azar flagellates. Of 70 volunteers who were inoculated with the ground-squirrel strain of L. donovani and examined 2 years later, none had developed kala-azar.

R. A. Neal

1093. Gamma-globulin and Acquired Immunity to Human Malaria

S. COHEN, I. A. McGregor, and S. CARRINGTON. *Nature* [Nature (Lond.)] **192**, 733-737, Nov. 25, 1961. 7 figs., 23 refs.

Infants born in hyperendemic malarial regions such as the Gambia are relatively resistant to malaria infection during the first 3 months of life; thereafter they suffer severe recurrent malarial attacks, which, however, become less frequent during later childhood. Acute clinical malaria is rarely seen in the adult.

In this study, γ globulin prepared from the serum of apparently immune adults by chromatography on columns of diethylaminoethyl cellulose was given intramuscularly at intervals of 8 to 24 hours for 3 days to 12 children aged 4 to 30 months who were suffering from acute malignant tertian malaria; the initial degree of parasitaemia was 10,000 to 230,000 per c.mm. Treatment was usually begun when the peripheral blood contained a high density of young ring-forms of the parasite. The total dose of γ globulin administered was 1.2 to 2.5 g., equivalent to 10 to 20% of the recipient's own γ globulin. Blood examinations were made at 12-hourly intervals.

On the 4th day after the beginning of treatment parasite counts were less than 1% of the initial figures; by the 9th day no trophozoites were present in 8 of the 12 patients. Temperatures fell gradually, and usually did not return to normal before the 7th day. There were no detectable changes in the morphology of the immature parasites appearing in the peripheral blood and there was no action against gametocytes. The globulin was effective against both Plasmodium falciparum and P. malariae, but the protection afforded was short-lived, the subjects being again susceptible to infection 3 months after treatment. Two children, who were admitted with pneumonia and measles respectively and who had relatively low malarial parasite densities, failed to respond to 1.2 g. of y globulin. The authors consider that the dosage of γ globulin in these patients was probably too

In further experiments children treated with γ -free fractions of Gambian serum or with γ globulin prepared from blood donors in Great Britain usually showed a decrease in trophozoite counts, but the responses were irregular and the mean counts between the 4th and 10th

days were considerably higher than those of patients treated with adult Gambian y globulin.

The rates of albumin and y-globulin synthesis were measured in Gambian adults exposed to infection, but without detectable parasitaemia, by using two isotopes of iodine, ¹³¹I and ¹²⁵I. Studies were made on similar subjects who had been protected for 4 or 5 years by antimalarial drugs, on West African students who had had malaria in childhood but had resided in England for 3 to 10 years, and on European subjects. The rate of synthesis of albumin was similar in all the groups, but the rate of y-globulin synthesis in unprotected, apparently healthy, Gambian adults was about 7 times that of Europeans. Prophylactic antimalarial drugs reduced the rate of synthesis, and residence in Britain reduced it still more. Nevertheless, West Africans resident in Britain still synthesize y globulin about twice as fast as healthy Europeans. The rate of synthesis was found to be low in an unprotected Gambian subject who was 3 months pregnant at the time of study; this observation may be related to the known increased susceptibility to malaria during pregnancy in hyperendemic areas.

These results show that immunity to malaria is similar to that acquired in other infections, being primarily dependent on protective antibodies associated with 7S γ -globulin. The antibody may act on mature intracellular parasites or on merozoites liberated from the erythrocytes. The slow development of immunity in hyperendemic areas is probably attributable to the poor antigenicity of serologically diverse strains of parasite, and it is likely that only a small part of the γ globulin synthesized in response to malaria is protective antibody.

L. G. Goodwin

1094. The Effect of Prednisone on Persistent Microfilaremia during Treatment with Diethylcarbamazine F. D. Schofield and R. E. Rowley. American Journal of Tropical Medicine and Hygiene [Amer. J. trop. Med. Hyg.] 10, 849-854, Nov., 1961. 20 refs.

Investigations were carried out in the Territory of Papua and New Guinea to ascertain why diethylcarbamazine treatment removes most microfilariae from the blood quickly, but often leaves a small minority still present. Seven men infected with microfilariae of Wuchereria bancrofti were given diethylcarbamazine, 1.5 mg. per kg. body weight 6-hourly for 6 days, when the average microfilaria count at 10 p.m. was reduced to 1.3% of its initial value. A similar group of 15 men were given prednisone, 0.15 mg. per kg., plus diethylcarbamazine, 1.5 mg. per kg., 6-hourly for 6 days, when the average microfilaria count was only reduced to 4.3% of its original value; when the prednisone was withdrawn and the diethylcarbamazine treatment continued for 3 more days the count fell to 2.6% of its initial value. Prednisone given alone for 24 hours did not affect the mean microfilarial count of the 15 patients or its periodicity. It is not clear whether the small number of microfilarae which persist after treatment with diethylcarbamazine (a) come from adult worms in ectopic sites in the body or (b) are resistant to a hypothetical antibody which might be involved in the microfilaricidal action of the F. Hawking

Allergy

1095. Effect of Glucocorticold Hormones on Experimentally Induced Allergic Reactions on Human Skin: a Histologic and Histochemical Study

R. E. MANCINI, P. A. COLOMBI, H. GALLI, and L. ORCIUOLL Journal of Allergy [J. Allergy] 32, 471–482, Nov.—Dec., 1961. 16 figs., 38 refs.

At the Institute of Allergy, Buenos Aires, 50 patients with pollen rhinitis or pollen asthma were divided into two groups, 21 being treated with prednisolone orally in a dosage of either 10 or 30 mg. daily for 1 to 30 days, while the other 29 were given topical treatment with various corticoid ointments 3 times a day for periods up to 9 months. In all patients 3 intradermal weals were induced, before and after treatment with saline, histamine, and pollen extract respectively, those in the patients using the ointments being induced in the treated area.

Histological and histochemical studies of skin biopsy specimens showed that after treatment there was less congestion and less serous and cellular exudate, dissociation of collagen and fragmentation of elastic fibres, atrophy of some fibroblasts, degranulation and partial vacuolization of mast cells. These changes were visible only after weeks or months of systemic or topical corticoid treatment, and in the main were similar also in the pollen, and histamine-induced weals.

H. Herxheimer

1096. Surgical Removal of the Carotid Body for Bron-

K. NAKAYAMA. Diseases of the Chest [Dis. Chest] 40, 595-604, Dec., 1961. 8 figs., 14 refs.

After a brief historical survey of the various surgical. procedures which have been tried in the treatment of asthma, the author reports the results obtained by excision of the carotid body, an operation which he first reported in 1942. The operative mortality is said to be negligible. The carotid body contains both mechanical pressorreceptors and chemoreceptors. In the intact man or rabbit the inhalation of 5% carbon dioxide leads to anincrease in the erythrocyte mass, but the author's experiments showed that this did not occur after bilateral removal of the carotid bodies. Similarly, following bilateral glomectomy the effect of the inhalation of sodium cyanide and lobeline upon the blood pressure was lost, as were also the respiratory responses to these drugs when injected weekly. Further, division of the - (nerves to the carotid bodies abolished respiratory reflex changes after intravenous injection of lobeline and sodium cyanide. Small doses of a local anaesthetic injected into the carotid body led to an increase in the erythrocyte count, but had no effect upon the blood pressure or respiratory reflexes; it is suggested that this effect is due to paralysis of sympathetic nerve fibres, and supports the notion of a relationship between carotid

body function and the autonomic nervous system. Finally-it was observed that following removal of the carotid body the patients often showed an increase in diaphragmatic respiration, with an increase in vital capacity and in arterial oxygen saturation. In hypertensive patients the blood pressure may fall after 6 months, while in hypotensive subjects it may rise. The serum adrenaline level rises and remains elevated for 3 weeks after the operation.

Up to 1949 excision of the carotid body was carried out in Japan in 3,914 cases of asthma, and in 2,535 of these there was said to have been marked to moderate improvement. In a survey of the author's own 1,013 cases (based on replies to a questionary) it was found that 72.6% showed good results 2 years after operation, and 58% up to 5 years after, while 16% of patients had no "postoperative episodes" of asthma. After 6 months the operative results of bilateral removal were no better than those of unilateral removal.

[Tables summarizing the results are quoted, but are nowhere to be found in the text. The assessment of the apeutic results based solely on answers to a questionary is apt to be misleading. It is surprising that bilateral excision of the carotid body is no more effective in asthmathan removal on one side only, especially when the effects on crythrocyte mass and respiratory and cardiovascular reflexes are observed only after bilateral removal.

R. S. Bruce Pearson

1097. Glomectomy for Asthma
R. H. OVERHOLT. Diseases of the Chest [Dis. Chest]
40, 605-610, Dec., 1961. 4 figs.

Influenced by the good results reported by Nakayama [see Abstract 1096] the author has, since May, 1958, treated 69 patients with intractable asthma by glomectomy (excision of the carotid body). The operation, which is described, is not severe and can be carried out under local anaesthesia. Information on 52 cases followed up for 6 months to over 2 years showed that some 80% of patients derived some benefit from the operation. Of 9 patients followed up for over 2 years, 4 were unchanged, but 3 were moderately, one significantly, and one markedly improved. Bronchospasm and rales persisted, however, and spirometric measurements were difficult to evaluate. The author concludes that "relief of bronchospasm is not the major contribution of glomectomy".

[Assessment of improvement in a study of this nature is always difficult. Unfortunately no case histories are recorded on which the reader could form some kind of judgment, nor are the criteria upon which the author made his assessment clearly stated. It is only possible to drawwalid conclusions in a series of this kind if it is compared with a similar series of control patients treated by orthodox methods. Also there is no mention of whether steroid therapy was given either before or after surgery.]

R. S. Bruce Pearson

Nutrition and Metabolism

1098. Cholesterol Drainage through a Choleretic Agent A. R. Olleros and C. M. Colon. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 438-444, Oct., 1961. 4 figs., 9 refs.

From the School of Pharmacy, University of Puerto Rico, the authors describe a new approach to the lowering of the serum cholesterol level which consists in stimulating increased physiological excretion of cholesterol by the liver. In experiments described they showed that when sodium dehydrocholate was given intravenously to rabbits-the physiological biliary excretion of cholesterol could be increased by 80% in comparison with normal control animals. In view of these experimental results 20 patients were then maintained on a cholesterol-poor diet and given a course of bile acid by mouth for 3 weeks in the form of various proprietary preparations. The serum cholesterol level in these patients had fallen on the average by 14% at the end of the course. On repetition of the same course a reduction in serum cholesterol level of 33% was obtained. The authors therefore recommend the use of choleretic agents in conjunction with other methods in the prophylaxis of atherosclerosis.

[For the reduction of serum cholesterol levels the following procedures are in use at present: diets restricted in fats, addition of essential fatty acids to the diet, and administration of oestrogen, thyroid hormones, sitosterols, nicotinic acid, triparanol, and choleretic agents.]

Z. A. Leitner

1099. An Isotope Test of Calcium Absorption S. D. Bhandarkar, M. M. Bluhm, J. MacGregor, and B. E. C. Nordin. *British Medical Journal [Brit. med. J.*] 2, 1539-1541, Dec. 9, 1961. 4 figs., 9 refs.

Up to the present the measurement of calcium absorption has required the performance of full calcium balance studies, which may take at least 3 to 4 weeks. In view of this the authors, in this preliminary communication from the University of Glasgow, describe an isotopic procedure for the estimation of calcium absorption which is based on plasma radioactivity 2 hours after the oral administration of the calcium isotope 47Ca. In carrying out the procedure 7.5 μ c. of ⁴⁷Ca (or in some subjects over 40 years of age 5 µc. of 45Ca) was equilibrated with a carrier, usually 250 mg. of calcium chloride, for 24 hours and then administered one hour after the last meal. Initially, blood samples on which to estimate activity were taken after 1, 2, and 3 hours, but when samples from the first 8 normal subjects showed a rise in activity for 2 hours, the level then remaining stationary, the activity at 2 hours was selected as the significant value. The series investigated included 34 normal subjects, 27 patients with osteoporosis from various causes, 21 with steatorrhoea, 12 patients receiving steroid therapy, and one with Cushing's disease. The isotope absorption test was carried out on 9 patients on whom calcium

balance studies were being performed concurrently and on 10 in whom the results of earlier balance studies performed the previous year were available. Good agreement was obtained between the two procedures.

In the normal subjects the 2-hour plasma activity showed 0.4 to 3% of the dose per litre of plasma, and results were similar in the case of osteoporosis. In the patients with steatorrhoea the findings were more difficult to evaluate, but they did not show any gross abnormality, it is noted, however, that there were no cases of untreated osteomalacia in this group. Lowered absorption occurred in patients receiving steroid therapy. In 10 cases the carrier employed was calcium carbonate (instead of calcium chloride) and absorption appeared to be reduced when this substance was used.

B. M. Ansell

1100. Acute Effects of Triparanol in Man D. H. Blankenhorn and O. Kuzma. Metabolism: Clinical and Experimental [Metabolism] 10, 763-770, Oct., 1961. 2 figs., 15 refs.

At the University of Southern California, Los Angeles, the authors have investigated the effects of triparanol on the blood sterol, triglyceride, and phospholipid levels in 6 patients taking an unselected diet. The drug, which interferes with the synthesis of cholesterol, was given in a dosage of either 250 mg. (4 cases) or 1 g. (2 cases) daily for 4 weeks, and the studies continued for a further 3 weeks after its withdrawal. Steroids were determined by ferric chloride colour reaction, by digitonin precipitation, and by micro-oxidation and the Liebermann-Burchard reaction.

In 5 of the 6 subjects there was a modest fall in the serum total sterol level; the values obtained by the three methods used differed slightly, but the magnitude of change was the same. By a simple modification of the Liebermann-Burchard reaction it was also possible to measure the serum desmosterol concentration, which was found to rise inevitably with triparanol therapy; as the long-term effects of desmosterol are unknown, the authors suggest that it is important to measure the level of this sterol in future studies of patients being treated with triparanol. The rise in the serum desmosterol level was independent of the dose of triparanol and not related in any simple manner to the magnitude of the decrease in the serum total sterol content. It is suggested that the best results from triparanol therapy might be obtained in those patients who experience the greatest fall in total sterol level and the least rise in that of desmosterol. In regard to the other blood fatty acids 2 of the patients showed a fall in the serum triglyceride level, but in the others no significant change was seen, while the serum phospholipid concentrations showed insignificant changes in all cases.

A further study on 2 out-patients showed that in one who had essential hypercholesterolaemia the serum total

sterol levels fell while he was taking triparanol, this being accompanied by a striking rise in the serum triglyceride level, which did not return to the pretreatment value within the 3 weeks after withdrawal of the drug. In the second patient, who had primary biliary cirrhosis, triparanol reduced the serum total sterol level without producing any marked rise in the serum desmosterol level, and the slight rise which did occur disappeared rapidly on withdrawal of the drug, suggesting that the ability to clear circulating sterols is not impaired in this disease.

A. Gordon Beckett

METABOLIC DISORDERS

1101. An Immunological Study of Coeliac Disease and Idiopathic Steatorrhoea: Serological Reactions to Gluten and Milk Proteins

K. B. TAYLOR, D. L. THOMSON, S. C. TRUELOVE, and R. WRIGHT. British Medical Journal [Brit. med. J.] 2, 1727-1731, Dec. 30, 1961. 2 figs., 21 refs.

An obstacle to the acceptance of the immunological theory of causation of coeliac disease and steatorrhoea has been the lack of satisfactory demonstration of antibodies to the protein concerned. This paper from the Radcliffe Infirmary, Oxford, therefore describes the results obtained when the sera from 24 children with coeliac disease and 45 adults with idiopathic steatorrhoea were examined for the presence of antibodies against a peptictryptic digest of wheat gluten, called by Frazer et al. (Lancet, 1959, 2, 252; Abstr. Wld Med., 1960, 27, 280) Fraction III, and also against various purified cow's milk proteins (casein, α -lactalbumin, and β -lactoglobulin). Control sera were obtained from 50 children and 64 adults. These sera were tested for antibodies against Fraction III by Ouchterlony's gel-diffusion precipitating technique, a standard complement fixation test, and a coated tanned-erythrocyte test. For antibodies against the individual proteins in cow's milk the coated tannederythrocyte test was used.

The sera of all patients and controls gave negative results with Fraction III in the gel-diffusion and the -complement fixation tests. By the coated tannederythrocyte test the sera of children with coeliac disease and adults with idiopathic steatorrhoea gave a significantly greater number of positive reactions against Fraction III and the individual milk proteins than did the control sera (P<0.01). In contrast, 15 adults with steatorrhoea following partial gastrectomy or secondary to pancreatic disease gave normal results. Positive reactions (titres of 1:200, 1:2,000, and 1:20,000) with Fraction III occurred in only 10 (20%) of sera from the control children, the other 40 (80%) giving negative or insignificant reactions (titre 1:20). Of the 24 children with coeliac disease, 15 (62.5%) gave positive reactions and 9 (37.5%) negative or insignificant reactions. Of 64 adult controls, 59 (92.2%) gave negative results and only 5 (7.8%) a positive reaction, while of the 45 adults with idiopathic steatorrhoea, 25 (55.6%) gave a negative result and 20 (44.4%) a positive result. There was similarly a scarcity of negative reactions and an excess of positive reactions when the sera from the patients with coeliac

disease and adult idiopathic steatorrhoea were tested with the individual milk proteins.

The authors discuss the significance of their findings in relation to the actiology and treatment of steatorrhoea, and suggest that the increased titres to Fraction III in such patients might be due to an increase in the absorption of an unchanged antigenic protein by the diseased intestinal mucosa.

Heweti A. Ellis

1102. Accidental Hypothermia H. Duguid, R. G. Simpson, and J. M. Stowers. Lancet [Lancet] 2, 1213-1219, Dec. 2, 1961. 8 figs., 28 refs.

The authors have studied a series of 23 cases of accidental hypothermia, which they define arbitrarily as rectal temperature below 90° F. (32·2° C.). They emphasize that such cases will be missed unless a low-reading rectal thermometer is employed as a routine when the ordinary clinical thermometer fails to register. All except 2 of the patients were over the age of 65, the youngest being a woman aged 56. They point out that three phases can be distinguished according to body temperature—namely: (1) 98 4 to 90° F. (36·9 to 32·2° C.), (2) 90° to 75° F. (32·2 to 23·9° C.), and (3) below 75° F. It would appear that the temperature reading when the patient is admitted is of some prognostic value.

The only abnormality revealed by a battery of laboratory tests was a raised serum amyiase level which could not be correlated satisfactorily with the pancreatic necrosis found in some of the patients. The routine treatment was to allow the patients to warm up gradually by simply wrapping them in blankets and keeping them at the ward's current ambient temperature. Antibiotics were given to all the patients, usually penicillin with or without streptomycin. Fluids were administered parenterally in almost all cases because consciousness was impaired or weakness was so marked that adequate fluid intake by mouth could not be ensured. Hydrocortisone was given, also parenterally, to many of the severely hypothermic or hypotensive patients, and vasoconstrictor drugs were used in most of the hypotensive cases in an effort to prevent renal cortical necrosis and irreversible damage to the brain. The authors cite evidence in support of the view that corticosteroids should be given in all cases of hypothermia and in substantial dosage. No single method or combination of methods of treatment could be adduced as proper for this condition, except when myxoedema was the cause of the hypothermic state (5 cases in the present series). Of the 23 patients, only 7 survived the episode of hypothermia. Necropsy findings were those typically seen in shock-like conditions-namely, acute gastric ulceration, acute pancreatitis, and visceral micro-infarcts. The authors' finally urge that "elderly patients with accidental hypothermia should not be actively rewarmed ".

[Accidental hypothermia is by no means rare in the aged and carries a very high mortality. Agreement has not yet been reached on the ideal way of treating these patients, but research is going on in many centres. Those particularly interested in the subject are recommended to read the original paper.] P. D. Bedford

Gastroenterology

STOMACH AND DUODENUM

1103. Esophageal Hiatal Hernia—a 10-Year Study of Medically Treated Cases

J. C. REX, H. A. Andersen, L. G. Bartholomew, and J. C. Cain. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 271-274, Oct. 21, 1961. 1 fig., 6 refs.

The course of oesophageal hiatal hernia not surgically treated was studied at the Mayo Clinic in 365 patients in whom the condition had been diagnosed 10 years previously. Although most of the patients had been instructed in a treatment regimen it was believed that few had adhered strictly to it. The hernia was of the sliding type in 301 of the patients, and 60% of these were symptom-free after 10 years; the remainder continued to have symptoms or had had surgical treatment. The size of the hernia bore little relationship to the severity of the symptoms or to their duration before the condition was diagnosed. The short-oesophagus type of hernia was present in 58 patients, of whom 27 still had symptoms at the end of 10 years and 9 had undergone surgery during that period. Only 6 patients (females) had the para-oesophageal type of hernia, which was always massive. However, none of these patients had needed surgical correction of the hernia and 4 were symptomfree.

Of the patients with sliding hernias, those with oesophagitis when first seen (70) improved less readily than those without, only 27 of the former being symptom-free after 10 years. Oesophagitis and peptic ulceration, however, were more common in the group with a short-oesophagus type of hernia; only 3 of the 30 examined oesophagoscopically had a normal oesophageal mucosa, while 18 had actual inflammation or ulceration and 9 had oesophageal strictures.

There were 75 deaths in the series, 70 of which did not appear to be related to the hernia; 2 patients died from carcinoma of the stomach, one from carcinoma of the oesophagus, and 2 from rupture of the oesophagus.

The authors consider that since so few patients with a sliding diaphragmatic hernia have significant symptoms after 10 years, surgical correction is rarely necessary. This treatment need only be considered where such a hernia is associated with persistent oesophagitis, dysphagia, regurgitation, or loss of blood.

J. Warwick Buckler

1104. Circulatory Dynamics during Experimentally Induced Dumping Reactions: with Special Reference to the Splanchnic Circulation and the Dye Method Employed for Splanchnic Blood Flow Estimation. [Monograph, in English]

H. CASTENFORS. Scandinavian Journal of Clinical and Laboratory Investigation [Scand. J. clin. Lab. Invest.] 13, 1-76, Suppl. 62, 1961. 27 figs., bibliography. 1105. Secretion of Blood Group Substances in Duodenal, Gastric and Stomal Ulcer, Gastric Carcinoma, and Diabetes Mellitus

R. Doll, H. Drane, and A. C. Newell. Gut [Gut] 2, 352-359, Dec., 1961. 12 refs.

An association between the ABO blood groups and gastro-intestinal disease has been reported by various workers, including the present authors, and it has been shown that stomal, duodenal, and gastric ulcers are more common in persons belonging to blood Group O than in those belonging to the other three blood groups. It was also shown that the individuals of each blood group could be separated into secretors and non-secretors. that is, those who have and those who have not the ability to secrete the blood group substances in the mucous secretions. More recently, a further association was discovered by Clarke et al. between duodenal ulcer and failure to secrete the blood group substances in the mucous secretions (Brit. med. J., 1956, 2, 725, and 1959, 1, 603; Abstr. Wld Med., 1957, 21, 357, and 1959, 26, 17). In the present study the authors have investigated the relative incidence of peptic ulcer (and some other). diseases which are known to be associated with one or other of the ABO blood groups) among secretors and non-secretors in the ABO blood groups. An individual's ability to secrete ABO blood group substances was tested by observing whether his saliva would prevent the agglutination of Group O erythrocytes by an extract of the seeds of *Ulex europaeus*; this extract reacts with the H antigen common to all the ABO blood groups and has been found to react with the saliva of all secretors, irrespective of the blood group to which they belong.

The ABO blood group and the ABH secretor status were determined at the Central Middlesex Hospital, London, in 368 patients with duodenal ulcer, 202 with gastric ulcer, 83 with a stomal ulcer, 105 with gastric cancer, 102 with diabetes mellitus, and a control group of 610 subjects, comprising 385 healthy subjects and 225 patients with other conditions. It was found that the proportion of non-secretors among the healthy subjects was 21.3% and among the patients suffering from other conditions it was 20.9%. Among patients with a stomal ulcer the proportion of non-secretors was 49%, among those with duodenal ulcer it was 37%, and among those with a gastric ulcer it was 31%. There were no significant differences in the proportion of non-secretors as between the blood Groups O, A, and B plus AB. The incidence of all three types of peptic ulcer was greater among non-secretors than among secretors, the mean relative incidences being 1.8:1 for duodenal ulcer and 1.42:1 for gastric ulcer. The mean relative incidence of duodenal ulcer among patients of blood Group O compared with that among those in blood Groups A or B plus AB was 1.48:1 for secretors, and 1.47:1 for nonsecretors. This finding confirms the finding by Clarke

et al. that the association between duodenal ulcer and blood Group O is not limited to secretors, but holds equally for non-secretors.

It can be concluded, therefore, that the effect associated with the different blood groups does not depend upon the presence of the blood group substances in the gastro-intestinal secretions. Also, the results suggest that the specific risks associated with blood Group O and with non-secretion are multiplicative, and that the mechanisms involved are related to one another. Comparison of the present results with those obtained in two large series reported by other authors shows close agreement for all groups in the three series. It is noted that in all three series the proportion of non-secretors was usually higher among womer, than among men in the various pathological groups. The other findings in this study suggest that there may be a slight increase in the risk of gastric cancer among non-secretors, but that the occurrence of diabetes mellitus is independent of ABH secretion. Joseph Parness

LIVER

1106. The Effect of Portacaval Shunt on Thrombocytopenia Associated with Portal Hypertension

B. H. SULLIVAN JR. and H. J. TUMEN. Annals of Internal Medicine [Ann. intern. Med.] 55, 598-603, Oct. [received Dec.], 1961. 12 refs.

In order to determine the effect of portacaval anastomosis upon the platelet count of patients with portal hypertension the case records of 25 patients (23 of them with hepatic cirrhosis) operated on at the Walter Reed General Hospital, Washington, D.C., were analysed. Preoperatively 18 of these patients had platelet counts below 150,000 per c.mm. The 7 patients with normal counts suffered no bleeding episodes after operation and showed no fall in platelet count when examined postoperatively. No consistent change occurred after operation in the patients with low preoperative platelet counts, in 11 of whom the count remained below 150,000 per c.mm.; the remaining 7 patients, however, showed a postoperative rise in the count to normal (>150,000 per c.mm.), the increase ranging from 15 to 600% of the preoperative value. Failure to obtain a rise in the platelet count could not be attributed to a failure of the operation to produce a significant fall in the portal pressure. Three patients bled from oesophageal varices after an apparently effective shunt operation, but no relationship could be established between the haemorrhage and a low platelet count. For the whole series the follow-up period ranged from one month to 9 years, but in half (13 cases) it was less than 6 months.

The authors point out that some patients with portal hypertension therefore appear not to manifest thrombocytopenia, but the reason for this is obscure. Establishment of an effective portacaval anastomosis is not necessarily associated with a rise in the platelet count. Presumably in some patients the results of portal hypertension on the spleen are irreversible so that "hypersplenism" with thrombocytopenia persists in spite of

the effective lowering of portal pressure. Very rarely purpura associated with thrombocytopenia may occur after an operation and may require splenectomy for its relief:

A. E. Read

1107. Gastric Ulcerative Lesions in the Course of Cirrhosis (Chronic Ulcer of Cruvellhier and Acute Ulceration) in the Absence of Treatment with Cortisone. (Les lesions ulcéreuses gastriques au cours des cirrhoses (ulcère chronique type Cruveilhier et ulcérations aiguës) en dehors de tout traitement cortisonique)

F. POTET, —. CONTE-MARTI, M. CONTE, and A. LAMB-LING. Archives des maladies de l'appareil digestif et des maladies de la nutrition [Arch. Mal. Appar. dig.] 50, 1038-1049, Oct., 1961. 4 figs., 28 refs.

Radiological and anatomical studies in 282 patients who had cirrhosis of the liver and who had not received cortisone, revealed the presence of chronic peptic ulceration in 35 cases (12.8%). In 21 of these patients there was a chronic gastric ulcer, usually situated on the lesser curvature, in 12 a duodenal ulcer, and in 2 both a duodenal and gastric ulcer. These ulcers seemed to be particularly liable to develop complications, even in the absence of cortisone therapy, and severe haemorrhage occurred in 10 cases and perforation in 5. Gastrectomy was performed in 16 cases. Details are also given of the gastric lesions found in 7 out of 76 patients (9.2%) with cirrhosis who came to necropsy. These lesions varied from simple acute erosions to more extensive necrotic and acute ulceration; they were found rather more frequently in patients who had received cortisone derivatives than in those who were not so treated.

A. W. H. Foxell

1108. An Evaluation of isoCitric Dehydrogenase in Liver Disease

N. N. COHEN, H. P. POTTER JR., and G. N. BOWERS JR. Annals of Internal Medicine [Ann. intern. Med.] 55, 604–609, Oct. [received Dec.], 1961. 2 figs., 10 refs.

Except in the presence of haemolysis a rise in the serum activity of the enzyme *iso*citric dehydrogenase (I.C.D.) is found only in liver cell disease. Because of this fact and the technical advantages of measuring activity of this enzyme compared with that of the serum transaminases the authors have examined at the University of Pennsylvania, Philadelphia, its value in the investigation of various types of liver disease.

In patients with viral hepatitis a 5-fold or greater elevation of the I.C.D. and the serum glutamic—oxalacetic transaminase levels was less often found than a similar elevation of the serum glutamic—pyruvic transaminase (S.G.P.T.) level, so that in viral disease I.C.D. activity seemed less sensitive in detecting this type of liver cell injury. In carcinoma of the liver a slightly more frequent elevation of I.C.D. activity was found, compared with both transaminases. In other disorders, such as active hepatic obstructive jaundice and fatty infiltration of the liver, no clear-cut difference in sensitivity could be established. No elevation of I.C.D. level occurred in simple heart failure unless there was hepatic necrosis, nor was the level raised in pulmonary infarction.

The authors conclude therefore that the determination of scrum isocitric dehydrogenase activity is a reliable test of liver cell function, but that it offers, apart from its greater specificity, no advantages over determination of the more conventional transaminases. Further, in some conditions such as viral hepatitis the elevation of isocitric dehydrogenase may be less than that of S.G.P.T.

- A. E. Read

1109. Advances in the Metabolism of Bilirubin
W. T. FOULK and L. J. SCHOENFIELD. Journal of the
American Medical Association [J. Amer. med. Ass.] 178,
398-401, Oct. 28, 1961. 17 refs.

INTESTINES

1110. Topical Sterold Therapy for Ulcerative Colitis: Report of Fifty Cases

C. H. Brown and M. Merlo. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 343-354, Sept., 1961. 3 figs., 12 refs.

At the Cleveland Clinic, Ohio, 50 patients, aged 21 to 50 years, received topical steroid therapy for ulcerative colitis. An enema containing 40 mg, of methylprednisolone in 100 to 250 ml. of tapwater was given and retained for 4 to 10 hours daily over a period of 14 to 21 days. Symptoms had been present for more than a year in 39 of the patients, the duration for the whole group ranging from a few months to 15 years. In half of the patients the entire colon was involved. The initial response to treatment was good in 39 patients, but those with extensive involvement tended to relapse and responded less well to re-treatment. The authors consider that topical therapy is of value when the disease is limited; a relapse occurred during an average followup period of 11 months in only 3 out of 13 patients with involvement of the rectum only. . Arnold Pines

1111. Exudative Enteropathy. I. A Comparative Study of Cr⁵¹Cl and I¹³¹PVP

M. E. Rubini and T. W. Sheehy. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 892-901, Dec., 1961. 5 figs., 7 refs.

The use of radioiodinated polyvinylpyrrolidone (131I–PVP) was first reported by Gordon (Lancet, 1959, 1, 325; Abstr. Wld Med., 1959, 26, 18) who showed that when this substance was given intravenously to normal subjects very little of it was excreted in the faeces. If, however, it did appear, this was evidence of a loss of plasma protein into the intestinal tract, or exudative enteropathy. Working at the U.S. Army Tropical Research Medical Laboratory, University of Puerto Rico, the present authors have compared the use of ¹³¹I–PVP with radioactive chromium chloride (⁵¹CrCl), the latter being an isotope which attaches itself to the serum albumin.

When injected intravenously both these substances showed a steady rate of disappearance from the plasma. Since ⁵¹CrCl was found to be taken up rapidly by plasma albumin on incubation, it was therefore given in

a dosage of 5 to 10 μ c. It appeared in the erythrocytes where it reached its maximum concentration in 2 days, and, like 131I-PVP, could be detected soon after in both the liver and the spleen. In the case of 131I-PVP, thyroid uptake was noticeable despite the blocking of the thyroid gland with Lugol's iodine. In normal subjects the daily faecal excretion of 51CrCl was found to be between 0.05 and 0.20% per day compared with about 0.5% per day for 131I-PVP. The rate of fall of 131I-PVP activity in the plasma was much more rapid than that of 51CrCl and this made it difficult to calculate a "131I-PVP clearance" rate with reference to intestinal protein loss. Certain difficulties were experienced with both techniques. Thus 51CrCl was found to be rapidly absorbed into glassware, and the long biological and physical half-life of 51Cr is a hazard. However, its slow plasma clearance allows for better quantitative assessment of protein loss. In the 131I-PVP technique the amount of free 131I and the variation in the size of the molecule may lead to error; it has been demonstrated that 131I-PVP may not detect a small abnormal loss of albumin.

The authors conclude that although both techniques may give an indication of abnormal protein loss into the gut, quantitative estimates are not possible. Determination of the plasma albumin levels and the dietary history therefore remain in their view the best guides.

J. S. Malpas

1112. Exudative Enteropathy. II. Observations in Tropical Sprue

M. E. RUBINI, T. W. SHERRY, W. H. MERONEY, and J. LOURO. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 902-907, Dec., 1961. 1 fig., 5 refs.

Using the two isotopic techniques described above [see Abstract 1111] the authors have investigated the loss of protein in the faeces of patients with tropical sprue, hockworm, cirrhosis of the liver, and one case of idiopathic enteropathy in a girl aged 3 years who presented with oedema and hypoalbuminaemia. In none of these patients was there an obvious cause for the hypoalbuminaemia, except impaired liver function in the cirrhotic group.

In the patient with idiopathic enteropathy a spontaneous remission occurred, the plasma albumin level returning to normal after completion of the studies without any cause being found. Increased faecal radioactivity was observed in the cases of tropical sprue when either technique was employed, while in the young patient with idiopathic azotorrhoea both techniques gave consistently high results. No abnormal loss was noted in patients with cirrhosis or hookworm disease, or in the controls. In the patients with cirrhosis or hookworm disease, care was taken to exclude intestinal bleeding which could vitiate the results.

The authors consider that although these studies confirmed the presence of an exudative protein-losing enteropathy in tropical sprue, they do not feel justified in attributing the cause of the hypoalbuminaemia entirely to this cause on the basis of the results obtained in this study.

J. S. Malpas

Cardiovascular System

1113. The Regression of Pulmonary Vascular Disease after the Creation of Pulmonary Stenosis

J. F. DAMMANN JR., J. A. McEACHEN, W. M. THOMPSON JR., R. SMITH, and W. H. MULLER JR. Journal of Thoracic and Cardiovascular Surgery [J. thorac. cardiovasc. Surg.] 42, 722-734, Dec., 1961. 8 figs., 6 refs.

During the past 10 years we have stenosed the pulmonary artery in 63 patients in whom the diagnosis of a simple or complex large ventricular defect had been made. The indications for surgery were congestive failure or evidence of progressive pulmonary vascular disease. The patients were classified into three groups: (1) children under 2 years with evidence of failure, (2) patients with lesions which at the time could not be corrected, and (3) older children with correctable ventricular defects but with markedly elevated pulmonary vascular resistance who would not tolerate curative surgery.

Eleven of these 63 patients have since been operated upon and their defects corrected. There were 4 fatalities, 3 due to the complex nature of the malformation and one to a reaction to use of the heart-lung machine. Among the 6 patients in Group I, the pulmonary bed was found to be normal in the 5 in whom biopsy material was available. Hemodynamic studies were in agreement. There were 5 patients in Group II whose defects were corrected. Hemodynamic data indicated a reduction in pulmonary vascular resistance. Final pulmonary artery pressures were close to normal and a comparison of the lung biopsy material indicated a marked improvement in the pulmonary vascular bed. No patients in Group III have been re-operated upon because sufficient time for vascular healing has not elapsed. However, interval catheterizations suggest a significant decrease in resistance in the 2 patients studied.

The data obtained in this series suggest that the stress which produces vascular disease is removed when the distal pulmonary artery pressure is lowered. The pulse pressure decreased and the systolic peak dampened out. —[Authors' summary.]

1114. Elective Cardiac Arrest: Its Effect on Myocardial Structure and Function

D. R. MILLER, P. RASMUSSEN, B. KLIONSKY, F. P. COSSMAN, and F. F. ALLBRITTEN JR. Annals of Surgery [Ann. Surg.] 154, 751–768, Nov., 1961. 16 figs., 42 refs.

In this investigation of the effects of elective cardiac arrest on myocardial structure and function, carried out at the University of Kansas School of Medicine, Kansas City, the authors have made use of histochemical and electron microscope studies of the myocardium of dogs, the animals being divided into various experimental groups.

In the first group myocardial infarction was produced by ligation of the circumflex branch of the left coronary artery and after one to 60 minutes potassium citrate solution was injected to produce cardiac arrest, specimens of the myocardium then being taken from both ischaemic and non-ischaemic areas and analysed for glycogen content. The second group of dogs were treated by whole body perfusion, with total cardiopulmonary bypass, and myocardial specimens again taken at varying times after the start of perfusion; these animals served as a control group. In the third group cardiac arrest by anoxia (cross-clamping of the aorta and pulmonary artery) was performed on similarly perfused dogs. In two further comparable experiments cardiac arrest with potassium and by anoxia plus cooling respectively was carried out as before and samples of myocardium similarly examined.

In the dogs subjected to coronary occlusion only there was sudden and total loss of glycogen from the myocardium within 5 to 15 minutes. At 15 to 20 minutes the myocardium showed rarefaction of nucleoplasm, and at one hour swelling was visible in all mitochondria. In the control group treated by perfusion only there was no significant myocardial change apart from some loss of contractile power ranging up to 20%. In the second perfused group, in which cardiac arrest was produced by anoxia, it was found that if the aorta was clamped for over an hour there were severe changes in cardiac function. Also changes in the nuclei of the muscle were observed after 30 minutes and these were of the same degree as in coronary occlusion after 5 to 15 minutes. In the group subjected to perfusion and potassium cardiac arrest there was some loss of myocardial contractile power, but this was not so severe as with anoxic arrest. Even after one hour the microscopical appearances of the myocardium were practically normal and there was considerable preservation of glycogen, possibly owing to chemical fixation by potassium. It was confirmed, however, that in these circumstances patches of necrosis may occur, as has been previously observed. In the last group treated by hypothermia and arrest by anoxia some impairment of cardiac function occurred after perfusion, but alteration of cell structure was not severe. After one hour at a body temperature of 30° C. the changes were comparable with those seen after 30 minutes of anoxia at normal body temperature. Myocardial glycogen content was not unduly depleted after half an hour and at one hour the amount lost was only about the same as that produced by 5 minutes of coronary occlusion. The greatest loss of glycogen was in the mid-myocardial region.

The authors discuss critically the interpretation of these findings. With coronary ligation there appears to be some irreversible damage at 20 minutes, which reaches its maximum in one hour. The rapid loss of glycogen in coronary occlusion makes it unwise to contrast anoxic arrest with occlusion; the partial retention of glycogen in anoxic arrest may mean that the metabolic changes are not comparable in the two forms. It is

pointed out that the presence of glycogen cannot be regarded as a test of viability of the cell.

[The results of these experiments require careful scrutiny if the inferences drawn are to be applied in practice.]

T. Holmes Sellors

1115. Open Intracardiac Operations: Use of Circulatory Arrest during Hypothermia Induced by Blood Cooling J. W. Kirklin, B. Dawson, R. A. Devloo, and R. A. Theye. *Annals of Surgery [Ann. Surg.]* 154, 769-776, Nov., 1961. 4 figs., 18 refs.

At the Mayo Clinic during the past 2 years 52 patients have undergone repair of intracardiac defects under hypothermia. The cooling was obtained by perfusion, and circulatory arrest was induced in all cases. The standard Mayo-Gibbon oxygenator was used with a heat exchanger in 29 cases, while in the remaining 23 a new machine for right and left ventricular by-pass as introduced by Drew was employed. The period of circulatory arrest and the degree of hypothermia varied considerably in individual cases. For example, the closure of a Potts anastomosis undertaken for repair of Fallot's tetralogy only required 10 minutes at 27° C., whereas transposition operations requiring an hour or more were performed at 12 or 13° C.

The procedure of cooling during perfusion has been simplified by the introduction of efficient heat exchangers, but experience is required to allow for the drift of temperature when the circulation and again when the perfusion are stopped. The authors, who are satisfied with the handling of cooling during pump oxygenator perfusion in its relation to the duration of circulatory arrest, reserve their opinion on the Drew technique. They are satisfied that 10 minutes' arrest at 28° C., 15 minutes at 22° C., and 30 minutes at 12 to 14° C. are safe, and have found the still, dry heart most suitable for the actual intracardiac operation, but in their view when there is a small pulmonary artery or when sutures have to be applied close to the A-V bundle a beating heart is to be preferred. T. Holmes Sellors

1116. A Technique for the Combination of Profound Hypothermia and Extracorporeal Circulation with Complete Circulatory Arrest

A. J. GUNNING. Thorax [Thorax] 16, 320-324, Dec., 1961. 4 figs., 2 refs.

In the technique employed for intracardiac operations at the Nuffield Department of Surgery, Radcliffe Infirmary, Oxford, since August, 1959, and here described, the heart-lung machine used is a Mayo-Gibbon vertical-screen oxygenator fitted with a heat exchanger, and the body temperature is lowed to 9 to 15° C. with complete circulatory arrest, thus allowing operation to be performed on a dry, still heart. A femoral artery and the right (and later the left) atrium are cannulated for the perfusion. A high flow rate is used throughout, and cooling is carried out slowly. Fibrillation occurs at about 25° C. and cardiac arrest at 20° C. After intracardiac surgery, which may take up to 70 minutes, the arterial flow is restairted and gradual rewarming begun. When the perfusion is stopped at about 35° C. the degree

of blood loss is estimated and corrected before the cannulae are removed. The venous pressure is a valuable aid in estimating blood loss, and the reminder is given that the blood in the open pleural cavity may easily be forgotten. A flow rate of 2 to 2.9 litres per minute persq. metre body surface is used. Adequate capillary perfusion is maintained throughout the cooling, "arfonad" (trimetaphan camphorsulphonate) being given as a vasodilator if necessary, so that the patient remains pink. At 15°C, the venous oxygen saturation approaches that in the arteries.

The results obtained with this technique in 32 operations for repair of a variety of congenital heart lesions, including transposition, are enumerated. There were no deaths or serious complications due to the perfusion or the hypothermia.

M. Meredith Brown

1117. The Technique of Hypothermic Perfusion P. J. Molloy and R. I. Lindfield. *Thorax* [Thorax] 16, 325-334, Dec., 1961. 4 figs., 21 refs.

The authors describe the machine, now in commercial production, which is used at Guy's Hospital, London, to provide extracorporeal circulation, with hypothermia to 15° C. Reservoirs receive coronary sinus blood by suction and venous blood from both venae cavae by gravity. A disk oxygenator provides 100% oxygenation at flow rates up to 2,800 ml. per minute. Through a roller pump the blood passes to a multi-tube heat exchanger which allows of both cooling and rewarming, and is returned to an external iliac artery. Controls and indicators are mounted on a convenient panel. Sterilization is achieved with ethylene dioxide gas. For priming the machine 2 litres of blood are required and to this heparin and calcium chloride are added.

When in use, the machine takes a gradually increasing amount of the cardiac output as cooling proceeds; the provision of a left atrial vent avoids overdistension. When total by-pass is achieved the pericardium is packed with ice. The resulting dry, still heart is available for up to 1½ hours. Rewarming is started slowly, and coronary arterial perfusion is used if the aorta has been opened. Heparin is neutralized with polybrene. Technical difficulties include overfilling, emptying due to failing venous return or blood loss, and rarely foaming or clotting of the blood. In practice the machine has been found to be versatile and easily controlled; it is compact, mobile, and quiet in operation. Further, it can be readily cleaned, the pumps are reliable, the disk oxygenator is safe, and all physiological requirements are met.

[Those wishing for more practical details should read the original article, where they are given in full.]

M. Meredith Brown

1118. The Results and Complications of Hypothermic Perfusion

P.J. MOLLOY. Thorax [Thorax] 16, 335-337, Dec., 1961: 8 refs.

In this paper the results in 194 patients treated at Guy's Hospital, London, by open heart surgery with extracorporeal circulation, are reported. Of this number,

61 (31.5%) died, but in the last 100 cases there were only 26 deaths.

Out of a group of 46 patients with aortic stenosis. mostly with calcification, there were 28 survivors. Among 39 patients with Fallot's tetralogy, there were 13 deaths, among 28 with ventricular septal defect 8 deaths, and among 20 with atrial sental defects only one death. There were no deaths among 10 patients with pulmonary stenosis, but in 8 operations for mitral regurgitation there were 6 deaths. By-pass time averaged 90 minutes. In regard to postoperative complications, several patients developed pulmonary congestion, sometimes needing tracheostomy, but cerebral complications were few. Some patients appear to have had acute tubular necrosis with renal failure, but all responded to treatment. - Postoperative bleeding was sometimes a severe problem, and widespread oozing was fatal in one case. Cardiac complications were unimportant. Acidosis was mild, but respiratory depression occurred several times. It is recommended that artificial ventilation should be carried out early. M. Meredith Brown

1119. Electrocardiography as a Means of Presaging Cardiac Pain

W. Evans. British Heart Journal [Brit. Heart J.] 23, 669-676, Nov., 1961. 8 figs., 4 refs.

In this paper from the London Hospital the author discusses the significance of the lesser electrocardiographic (ECG) changes indicative of limited cardiac infarction. As in previous studies he used four standard limb leads and the bipolar chest leads CR1, CR4, and CR7, considering the latter to portray more clearly the lesser ECG changes than do unipolar V leads.

Among the ECG records of 5,000 consecutive cardiological examinations in adults aged over 35 he found 108 symptomless and apparently healthy subjects who had an abnormal electrocardiogram, consistent with a myo-cardial lesion. Despite the abnormality these patients were reassured and not recalled for examination. As time passed, the subsequent progress in 57 of these became known. In 27 of them (23 men) cardiac pain had set in, but in the remaining 30, pain continued to be absent. The interval elapsing between the first visit and the onset of cardiac pain was 3 years or less in 13 cases and longer than three 3 in 14. Of the 27 with cardiac pain, 12 died within an average period of 3 years after the first examination.

He suggests that in a patient showing the lesser cardiographic signs of a myocardial lesion in the absence of pain, an ECG recorded after exercise will decide the imminence of the symptom. A strongly "positive" result indicates its early appearance, while if the result is negative or shows only very slight change after exercise pain may not trouble the patient for some years. The author states that he has yet to see a patient with pain associated with cardiac infarction whose ECG, recorded fortuitously within 3 years of onset of the pain, proved to be strictly normal. He concludes that "graphomancy" (or divination of cardiac pain) through the agency of the electrocardiogram is a reality.

T. Semple

CONGENITAL HEART DISEASE

1120. The Surgical Treatment of the Tetralogy of Fallot C. N. Barnard and V. Schriffe. *Thorax* [Thorax] 16, 346-355, Dec., 1961. 4 figs., 35 refs.

In this paper from the Groote Schuur Hospital and the University of Capetown the authors report a series of 44 patients with the tetralogy of Fallot operated on under cardiac by-pass with a bubble oxygenator. Complete repair of the defect was attempted in all except 2 of the patients, and the importance of adequately relieving the obstruction to the pulmonary outflow tract is emphasized. Failure to relieve the stenosis was responsible for 3 of the 7 deaths in the 42 patients in whom a complete repair was attempted. In 10 patients infundibular resection and/or pulmonary valvotomy was carried out and in the remaining 32 a plastic repair of the pulmonary outflow tract was performed, "ivalon" being used in 4 and woven "teflon" in 28. The prosthesis was situated in the right ventricle in 13 cases, across the valve ring in 10, and extended as far as the bifurcation of the pulmonary artery in 9. In the first 10 patients heart block was produced twice, but in the last 32 patients, when the authors used the technique described by Kirklin et al. (J. thorac. cardiovasc. Surg., 1960, 40, 763) for suture of the defect, heart block was produced once only. In the surviving patients the clinical response to surgery was gratifying. Effort tolerance was restored to normal, and recatheterization of the first 14 patients revealed a satisfactory haemodynamic state in the majority.

The authors conclude that patients with Fallot's tetralogy may be divided into: (1) those with adequate outflow tract development distal to the stenosis, which may be relieved by infundibular resection and/or pulmonary valvotomy; and (2) those with inadequate outflow tract development, which must be relieved by a patch of plastic material in the right ventricle, extending if necessary across the pulmonary valve and even as far as the bifurcation of the main pulmonary artery. They recommend a "two-stage" procedure for the few exceptional cases in which the hypoplasia extends into the small pulmonary arteries and cannot be relieved by a plastic repair.

R. L. Hurt

1121. Tricuspid Atresia and Its Prognosis with and without Surgical Treatment

M. CAMPBELL. British Heart Journal [Brit. Heart J.] 23, 699-710, Nov., 1961. 4 figs., 24 refs.

This is a further classic treatise by the author on a less common form of congenital heart disease. During the period 1947-51 the diagnosis of tricuspid atresia was made in 31 (5%) of 670 patients seen at Guy's Hospital, London, with cyanotic congenital heart disease. The mortality is high even after infancy, and was estimated at 30% within 5 years of the patients' being first seen. The triad of central cyanosis, a diminutive right ventricle, and left axis deviation, often with a large P wave in Lead II, leads to its recognition. Radiologically, most of the antero-posterior films show the heart to be of a characteristic shape, this resulting from the relative absence of the right ventricle. Angiocardiography is of great value in

confirming the diagnosis, the passage of blood from the right to the left atrium being clearly shown. Cardiac catheterization is not generally of much value. Besides the original 31 cases, 9 seen later are also considered in discussing the outcome.

Of 28 patients who did not have an operation, 20 died. all but 5 of these doing so within 2 years of being first seen; only one lived for more than 6 years. Surgical treatment was carried out in 12 patients, of whom 7 are greatly improved after 7 to 10 years. Of the others, 3 died within a year or so and 2 died after being improved for 6 years. In discussion the author notes that a few patients with this malformation have only slight disability and cyanosis. In these cases the blood flow to the lungs is adequate, but not too large, as may happen when the ventricular septal defect is large enough to allow an adequate flow to the right ventricle or when the pulmonary trunk arises from the left ventricle and is, suitably stenosed. He suggests that, apart from these few, all other such patients should be given the chance of a subclavian-pulmonary artery anastomosis.

T. Semple

1122. The Differential Diagnosis of Congenital Heart Disease. I. Lesions with No Shunt

A. M. LANSING. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 1335-1339, Dec. 16, 1961. 1 fig., 5 refs.

VALVULAR DISEASE

1123. Intracardíac Acetylcholine Infusion and Left Heart Dynamics in Rheumatic Heart Disease

P. SAMET, W. H. BERNSTEIN, and R. S. LITWAK. British Heart Journal [Brit. Heart J.] 23, 616-620, Nov., 1961. 2 figs., 6 refs.

Right heart acetylcholine infusion was employed in the course of combined right and left heart catheterization in 14 patients with rheumatic heart disease. Left atrial mean pressure and the mean diastolic mitral gradient and the mean systolic aortic gradient were not altered by acetylcholine infusion. Pulmonary arterial pressure fell only slightly after acetylcholine infusion. Acetylcholine offers little promise as a clinically useful pulmonary vasodilator agent.—[Authors' summary.]

1124. Aortic Stenosis and Unexplained Gastrointestinal Bleeding

R. C. WILLIAMS JR. Archives of Internal Medicine [Arch. intern. Med.] 108, 859–863, Dec., 1961. 20 refs.

Out of a consecutive series of 1,443 patients admitted to the Massachusetts General Hospital with gastro-intestinal bleeding and a concurrent anaemia of 10 g. haemoglobin per 100 ml. or less, 95 (6.6%) had no demonstrable bleeding site. Of these, 24 (25.5%) were found to be suffering from aortic stenosis. This incidence is significantly different from that of a group of patients matched for age and sex admitted for other reasons and also from those patients who had bleeding from known sources. In both these latter groups the incidence of aortic stenosis was about 5%. Of the 24 patients with

unexplained bleeding, 16 were between the ages of 70 and 89. A positive serological reaction for syphilis was obtained in 17% of this group. Diabetes mellitus was present in 28%. During episodes of bleeding the pulse pressure tended to narrow.

It would appear that patients with aortic stenosis and unexplained gastro-intestinal bleeding are liable to suffer repeated and severe episodes of bleeding. During these episodes they are more liable to develop angina and weakness than congestive heart failure.

E. H. Johnson

1125. The Clinical, Hemodynamic, and Pathologic Diagnosis of Muscular Subvalvular Aortic Stenosis

H. Menges Jr., R. O. Brandenburg, and A. L. Brown Jr. *Circulation* [Circulation] 24, 1126-1136, Nov., 1961. 11 figs., 20 refs.

In this study from the Mayo Clinic 8 cases of proved muscular subvalvular aortic stenosis are presented. In 3 cases necropsy was performed, while in 5 cases the diagnosis was established at operation. The clinical features of the condition are described in detail, with special attention to the auscultatory and phonocardiographic findings. It is pointed out that the presence of a diastolic murmur would make the diagnosis of outflow obstruction most unlikely. The electrocardiogram in 7 of the 8 cases showed left ventricular hypertrophy of the pressure overload type and, radiologically, ventricular enlargement was present in all cases. There was, however, no elevation of blood pressure or evidence of other disease that might predispose to cardiac hypertrophy.

The diagnosis in this condition is confirmed accurately by cardiac catheterization, the most reliable criterion being the presence of a zone of reduced systolic pressure in the infundibulum of the left ventricle. As the catheter is withdrawn across the narrowed outflow area the systolic pressure falls, but the diastolic level remains unchanged. When the aortic valve is traversed the diastolic pressure rises, but the systolic pressure remains unaltered. Another consistent finding in the present series was the presence of a notch on the ascending limb of the left ventricular pressure tracing. The exact mechanism of this phenomenon is not clear. The pathological findings at operation and at necropsy showed that the muscular septum was at least 11 times as thick as the left ventricle, a proportion far beyond that in a control series of 50 hypertrophied and 20 apparently normal hearts, studied in consecutive order at necropsy. In the 3 specimens examined histologically no significant abnormality was noted.

Present information is not sufficient to enable any positive conclusions to be drawn as to the aetiology of the condition, although familial and developmental factors appear to be implicated.

P. T. O'Farrell

1126. The Third Heart Sound in Mitral Regurgitation P. G. F. Nixon. British Heart Journal [Brit. Heart J.] 23, 677-689, Nov., 1961. 8 figs., bibliography.

This paper describes an investigation carried out at the General Infirmary at Leeds of the origin of the third heart sound or protodiastolic gallop rhythm of mitral regurgitation. In 23 patients with chronic rheumatic mitral valvular disease left heart pressures were recorded by catheterization through the atrial septum, while simultaneous tracings were made of arterial pressure, heart sounds, and the electrocardiogram.

Third heart sounds were present in the majority of heart cycles in patients with mitral regurgitation, but were absent in those with mitral stenosis or stenosis with regurgitation. In every case the interval between closure of the aortic valve and the third heart sound equalled the interval between aortic valve closure and the left atrial annular ascent point, when averaged over 10 hearts. The changes in left atrial pressure occurring at the annular ascent point are thought to be caused by ascent of the mitral annular fibrosis and consequent reduction of the mitral orifice. A physiological third heart sound also coincides with the annular ascent point and probably also originates from sudden tautening of the mitral cusps and chordae. An audible third heart sound is an important feature of mitral regurgitation, hypertension, ischaemic heart disease, and cardiomyopathy; elevation of the left ventricular end-diastolic pressure is common to all of these. It may be that ventricular distension is responsible for increasing the tension in the cusps and chordae in such cases. Audibility of a physiological third heart sound is not easy to explain, but it may be that the left ventricular residual volume is relatively great in T. Semple . the youthful heart.

1127. The Role of Surgery in the Treatment of Mitral Regurgitation

E. B. KAY, D. MENDELSOHN JR., and H. A. ZIMMERMAN. *Progress in Cardiovascular Diseases* [*Prog. cardiovasc. Dis.*] 4, 259–269, Nov., 1961 [received Jan., 1962]. 7 figs., 17 refs.

In the authors' view the role of surgery in the treatment of mitral incompetence depends on the clinical course of the untreated condition and the likelihood of benefit from surgery. They discuss the diagnosis of regurgitation and stress the importance of periodic objective examinations. Surgery has shown that the condition is often not so benign as was hitherto thought to be the case, and the good results obtained have made accurate diagnosis and assessment more important.

The pathology of the valve lesions in 146 patients in whom mitral regurgitation was corrected at St. Vincent Charity Hospital, Cleveland, Ohio, is described. Of these patients, 23% had pure regurgitation, 34% had some stenosis but predominant regurgitation, 29% had dominant stenosis, and 14% had virtually destroyed valves. It is pointed out that the results of surgery today are such that it is no longer necessary to wait until a patient is gravely disabled before operation is recommended; in fact, the earlier in the course of the disease it is carried out, the better the result. The authors now operate on all cases of mitral valve disease by the open method since they have obtained better haemodynamic results with this than with closed techniques.

Their methods, which are briefly described, consist in suturing tears, annular plication, or the reconstruction

of the chordae tendinae. Although the methods are not yet perfect, at least 80% of their patients have benefited clinically from operation.

J. R. Belcher

1128. Recent Developments in the Surgical Treatment of Mitral Stenosis

C. P. Balley. Progress in Cardiovascular Diseases [Prog. cardiovasc. Dis.] 4, 270-277, Nov., 1961 [received Jan., 1962]. 2 figs., 14 refs.

The author advances arguments against the closed method of treatment of mitral stenosis—namely, valve mobilization may be incomplete, there is a certain incidence of traumatic mitral incompetence, the risk of embolism, there may be dominant incompetence, and finally the high incidence of re-stenosis. [He does not explain why some of these risks will be diminished by open operation.] He considers that a re-stenosis rate of 25% is conservative and points out that mortality at the second operation has been estimated by some workers to be as high as 50% [both these figures are gross overestimates]. He reasons that only 43 to 70% of patients subjected to the closed operation "are permanently benefited".

At the Flower and Fifth Avenue Hospitals, New York, the author's method of approach consists in a left thoracotomy with cannulation of the pulmonary artery and the descending aorta. The valve is mobilized as fully as possible under direct vision and any incompetence is corrected. The steps required to avoid air embolism are described, although it was responsible for 3 of the 6 deaths in a series of 42 patients operated on. Half of the patients had some element of incompetence at the end of the operation, but in none was it significant [the results in terms of exercise tolerance are not given].

J. R. Belcher

1129. Effects of Acetylcholine on Hemodynamics and Blood Oxygen Saturation in Mitral Stenosis C. A. Stanfield, J. K. Finlayson, M. N. Luria, H.

C. A. STANFIELD, J. K. FINLAYSON, M. N. LURIA, H. CONSTANTINE, F. J. FLATLEY, and P. N. Yu. *Circulation [Circulation]* 24, 1164–1172, Nov., 1961. 23 refs.

Haemodynamic and blood gas estimations and respiratory function tests were undertaken during cardiac catheterization in a group of 18 patients with mitral stenosis before and at the same time as infusion of acetylcholine into the pulmonary artery at a rate of 2 to 12 mg. a minute, just insufficient to produce coughing or wheezing. Acetylcholine produced a significant decrease in pulmonary resistance, pulmonary arterial pressure, and systemic arterial oxygen saturation in half of the patients, usually associated with increased cardiac index and "central" blood volume. In the other patients there was no significant desaturation of systemic arterial blood and the changes in the other parameters were minimal or in the opposite direction to those recorded in the first group.

From a consideration of the data the authors rule out such possible explanations for systemic arterial desaturation in the first group as decreased alveolar ventilation, focal bronchoconstriction, or opening up of pulmonary arterio-venous shunts by-passing the alveoli and suggest that the most likely explanation was an increased pulmonary blood flow in pre-existing poorly ventilated regions of the lungs as a consequence of pulmonary arteriolar dilatation.

K. G. Lowe

1130. Left Bronchial and Pulmonary Changes in Mitral Stenosis

H. VESELL. Diseases of the Chest [Dis. Chest] 40, 557-563, Nov., 1961. 4 figs.

The bronchial and pulmonary changes which can occur in mitral stenosis are described with reference to the findings in 4 cases seen at the Beth Israel Hospital, New York. Anatomical changes due to enlargement of the left atrium include widening of the angle of bifurcation at the bronchial origin and elevation of the left bronchus. At 2 to 3 cm. distal to the origin of the left bronchus there may be a further elevation, either abruptly or in a curve. There may also be a backward displacement. These same anatomical factors may compress the left main bronchus, this compression being increased by thickening of the wall from congestion and inflammation and by secretion into the lumen. Pulmonary parenchymal changes are always present in severe mitral stenosis; they are due to direct pressure, increased pulmonary venous pressure, or repeated infection.

Surgical treatment of the stenosis by removing much of the cause can relieve the symptoms. In one of the cases described valvotomy and lobectomy for bronchiectasis in the left lower lobe were followed by considerable improvement.

E. H. Johnson

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1131. The Natural History of Ischaemic Cardiopathy Due to Coronary Atherosclerosis. (L'histoire naturelle des cardiopathies ischémiques par athérosclerose coronarienne)

J. LENEGRE, J. HIMBERT, R. FROMENT, J. NORMAND, and A. PERRIN. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 37, 3336-3342, Dec. 2, 1961. Bibliography.

This paper from the Hôpital Boucicaut, Paris, and the Hôpital Edouard-Herriot, Lyons, is based on a joint retrospective post-mortem series of 462 cases of ischaemic heart disease due to coronary atherosclerosis. The onset of the disease was in the form of angina pectoris in 54% of the cases, of protracted pain with myocardial infarction in 24%, and without pain (often with heart failure) in 22%. The average age at onset was 57 years, with only 3% of the patients aged under 40 years and 18% under 50. In men the disease began on the average 10 years earlier than in women. In about half the cases angina of effort appeared suddenly, suggesting the possibility of coronary thrombosis, but increased progressively in the other half. Later the pain may disappear, only to recur after 1 to 6 years, or the attacks may multiply, finally resulting in anginal status with myocardial infarction or sudden death. Myocardial infarction appeared suddenly in previously healthy subjects in 47% of the cases, the remaining 53% being

patients already suffering from angina pectoris; the more severe cases occurred in the former group.

The symptomatology varied: in 68% of the cases there was protracted angina pectoris, in 18% ordinary angina of effort, and pain was entirely absent in 14%. Heart failure, at first left ventricular and later global. almost invariably followed coronary atherosclerosis. In 50% of the cases heart failure followed angina of effort, in 22%: t was simultaneous with the onset of angina, and in 28% there was no antecedent angina. The evolution of this type of heart failure is usually severe; the authors have found that in half the cases it cannot be controlled and recurs shortly afterwards, constituting the direct cause of death. The average age at death was 63 years. the mortality being at its maximum at the beginning of the disease; 10% died during the first 6 weeks, and 30%. in one series and 50% in the other within the first year; the mean duration of the disease from onset was 4 years 11 months. That is, coronary atherosclerosis develops during an average of 5 years and ends with chronic and progressive heart failure in 31% of the cases, rapidly fatal myocardial infarction in 40%, and sudden death in 14% of patients.

1132. Oral Fat Tolerance in Young Men with Coronary Heart Disease

L. J. STUTMAN, M. GEORGE, L. G. GOTTSCH, and M. M. GERTLEE. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 736-745, Dec., 1961. 5 figs., 20 refs.

A comparative study of fat tolerance in men with and without coronary heart disease is reported from New York University Medical Center, the patients being 40 years old or younger and drawn from a large U.S.A.F. hospital. Special oral fat loading tests were carried out in 13 of the patients who had "pure" coronary disease and in 10 age-matched controls without discernible coronary disease.

It was found that in the 9-hour blood specimen the serum optical density in the patients with coronary disease was significantly raised and that over the whole time of testing the total fatty acid and cholesterol levels in this group were much higher than in the controls. In addition there was a delay of 3 hours in the return to normal of the serum fatty acid level in the patients who, on prolonged food deprivation, showed a rise in serum fatty acid and β -lipoprotein levels at a time when there was a continuing decrease in controls. J. B. Wilson

1133. Ventricular Aneurysm: Fourteen Cases Subjected to Cardiac Bypass Repair Using the Pump Oxygenator D. W. Chapman, K. Amad, and D. A. Cooley. American Journal of Cardiology [Amer. J. Cardiol.] 8, 633-648, Nov., 1961. 14 figs., 28 refs.

The clinical features in 14 cases in which aneurysmal dilatation of the ventricle wall developed as a sequel to myocardial infarction are described in this paper from the Baylor University College of Medicine, Houston, Texas. The presenting symptoms were anginal attacks, episodic cardiac arrhythmias, exertional dyspnoea, and left heart failure. Catheter studies revealed reduced

cardiac output and significant pulmonary hypertension. Surgical excision of the inert fibrous sac, which always threatens as a dangerous nidus of embolization, was carried out in all cases. The technique consisted in cannulation of the cavae and ascending aorta through the femoral vessels before cardiac dissection and subsequent maintenance of circulation through a pump oxygenator at 35 to 50 ml. a minute per kg. body weight; the maximum total flow did not exceed 3,000 ml. a minute.

The authors state that excision of the aneurysm, ideally 3 months or longer after the infarction, permits suture of the ventricle through firm fibrous tissue. It gave symptomatic relief in 11 surviving patients. C. A. Jackson

1134. Observations on the Immediate Prognosis of Acute Myocardial Infarction

R. F. REINFRANK, D. E. HOLDSWORTH, and P. H. TWADDLE. Journal of Chronic Diseases [J. chron. Dis.] 14, 426-441, Oct., 1961. 1 fig., 7 refs.

This paper reports an analysis of the records of 350 cases (253 in males) of confirmed acute myocardial infarction admitted to Hartford Hospital, Connecticut, over a period of 20 months. These cases were divided into three groups, as follows. (1) Uncomplicated, in which the patient was alive 30 days after the infarction and showed no major complications between the 3rd and the 30th day after admission. (2) Complicated, that is, those alive on the 30th day but having suffered one of the following major complications—shock, congestive cardiac failure or pulmonary oedema, significant arrhythmias, recurrent cardiac pain, thromboembolic phenomena. (3) Fatal, in which the patients died during the first 30 days. Group 1 comprised 212 patients, of whom 49 had had a previous myocardial infarction, Group 2 68 patients, of whom 27 had had a previous infarction, while of the 70 patients in Group 3, 32 had had one or more previous infarctions. The immediate death rate (within 30 days) was significantly higher (46%) than the over-all rate of 20% for the entire series.

In regard to individual factors, of 37 patients with a previous history of congestive cardiac failure, 16 died (mortality 43%), of 98 with angina pectoris, 35 died (36%), and of 108 with previous infarctions, 32 (30%) died; the latter two factors, however, only assumed significance when associated with other items in the history. The presence of shock, congestive cardiac failure; or severe persistent cardiac pain markedly increased the immediate mortality. The death rate in those patients with a serum glutamic-oxalacetic transaminase level of 350 units or more was increased only when this raised level was associated with shock, heart failure, or arrhythmias. A leucocyte count above 15,000 per c.mm. was associated with a higher mortality rate (41%), but there was no quantitative relationship. A normal leucocyte-count, however, was related to a mortality rate half that of the whole series, as was also a normal body temperature. An elevated or depressed body temperature had no prognostic significance, nor had the erythrocyte sedimentation rate or the serum cholesterol level. In non-diabetic patients with fasting blood sugar levels above normal on admission the mortality was 30%, compared with 12%;

for those with normal blood sugar levels. Classification of the patients according to whether anticoagulant control was poor or good showed that among 119 patients in whom control was poor the mortality was 5.1% and incidence of thromboembolic complications nil, compared with a mortality of 14.2% among the 155 patients thought to be well controlled on anticoagulants, of whom 5 (3.2%) had thromboembolism. Of 43 patients who survived the first week and did not receive anticoagulant treatment, 9 died, representing a mortality of 21%, a rate indistinguishable from that for the whole series (20%).

The authors conclude that the prognostic features in acute myocardial infarction are so numerous that no one particular feature in the past history, physical complications, or results of laboratory investigations may be relied upon. They advocate a simple scoring system for all the significant factors at the time of onset and present details of a prognostic index rating.

J. Warvick Buckler

1135. Anticoagulant Therapy in the Relatively Young Male with Myocardial Infarction

J. E. Myers Jr. and F. L. BAUER. Annals of Internal Medicine [Ann. intern. Med.] 55, 760-764, Nov., 1961. 19 refs.

A total of 103 males under the age of 60 years were admitted to De Witt Army Hospital, Fort Belvoir, Virginia, with myocardial infarction between January, 1956, and October, 1960. Three died within 11 hours; of the remainder, 50 were treated with anticoagulants and 50 were not. The treated group consisted of 34 patients admitted between January, 1956, and September, 1958, and 16 admitted between May and December, 1960, those not treated being admitted in the interim period. The anticoagulants used were heparin initially, followed by a coumarin derivative, usually warfarin sodium. The average age of the treated patients was 44.2 years and of the controls 44.4 years, and the two groups were considered to be evenly matched, according to the changes in the electrocardiograms, as to the size and location of the lesions. However, 19 of the treated patients and only 10 of the untreated patients developed congestive failure, hypotension, shock, or arrhythmia, suggesting that the treated group contained several patients with larger and more severe infarctions than the average.

One patient who was not receiving anticoagulants died 68 hours after admission, but there were no other deaths within the 3-month follow-up period. For the whole series, including the 3 early deaths, the mortality was 3-8%. Extension of infarction occurred in 4 patients (8%) in each group and at the end of 3 months 27 patients treated with anticoagulants and 22 in the control group complained of angina. Pulmonary embolism was more frequent in the treated group (7 or 8%) than in the control group (1 or 2%), and the total thromboembolic complication rate was 18% in the former and 16% in the latter.

In this series the mortality rate was low and anticoagulant therapy was of no significant benefit. The authors therefore conclude that anticoagulants should not be prescribed for young patients with myocardial infarction who are otherwise healthy.

Eirian Williams

1136. Long-term Anticoagulant Therapy after Acute Myocardial Infarction: a Retrospective Study Based upon a Nine-year Experience at the University of Chicago P. R. Kuhn, A. L. Van Ness, R. J. Jones, and E. B. Bay. Archives of Internal Medicine [Arch. intern. Med.] 108, 884–896, Dec., 1961. 3 figs., 22 refs.—

Over a period of 12 years 736 patients were treated at the University of Chicago Clinics for acute myocardial a infarction. The diagnosis was established clinically and by electrocardiography. Of the 601 patients who survived the initial 6 weeks, 583 were observed until death or over a period of 2 years. During this period 166 patients (Group 1) were treated with anticoagulant therapy, most of them receiving bishydroxycoumarin. The aim of treatment was to maintain the prothrombin time at a level 2 to 3 times greater than that of a control group (Group 2) made up of 270 of the patients who did not receive anticoagulants after the initial 6-week period. The remaining 147 patients (Group 3) received anticoagulant therapy for part of the time." Many of them were asymptomatic after a period and stopped treatment. Others who had been in the control group were given anticoagulants because of repeated infarction.

The mortality for the 2-year period in Group 2 was 26% and in Group 1 13%. This significant difference persisted in various subgroups, except for diabetics, among whom the death rate was the same for those receiving anticoagulants and for controls. The greatest effect was seen in patients who had had more than one infarction, the death rate for those treated being 14% compared with 41% in Group 2. Analysis of Group 3 confirmed the value of long-term therapy, 14 of the 17 deaths in this group occurring after the cessation of treatment.

There is evidence that the sudden withdrawal of anticoagulants may cause rebound thrombo-embolism. Half of the 18 patients who had recurrent attacks of myocardial infarction while receiving treatment were found to have a prothrombin time below the therapeutic level.

E. H. Johnson

1137. The Physiopathology of Hypertensive Attacks in Myocardial Infarction. (Les poussées hypertensives au cours de l'infarctus du myocarde. Leur physiopathologie)

P. Broustet, H. Bricaud, P. Blanchot, J. de Lostalot, G. Cabanieu, M. Dallocchio, and M. Trarieux. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 37, 2968–2972, Nov. 2, 1961. 31 refs.

On the basis of 22 cases seen at Bordeaux in the past 2 years the authors assert that arterial hypotension is an essential and indeed an almost constant sign of myocardial infarction and in their experience is often preceded by a rise in arterial pressure. This hypertensive attack may last from 2 to 12 hours and varies greatly in severity. These patients appear to have a particularly good prognosis. To explain the mechanism of this phenomenon, the authors have worked out a theory of increased production of adrenaline and noradrenaline initiated by the pain itself. Some of the pressor amines are released from the necrotic myocardium, apparently in the same

way as are the transaminases. [The authors present no actual laboratory proof for their interesting hypothesis.]

A. I. Suchett-Kaye

1138. Disorders of Atrio-ventricular Conduction in Recent Myocardial Infarction. I. Clinical Study. (Les troubles de la conduction auriculo-ventriculaire dans l'infarctus myocardique récent. I. Étude clinique) M. BLONDEAU, P. RIZZON, and J. LENÈGRE. Archives des maladies du cœur et des vaisseaux [Arch. Mal. Cœur] 54, 1092-1103, Oct. [received Dec.], 1961. 5 figs.

Among 552 patients with cardiac infarction admitted to the Hôpital Boucicaut, Paris, in the course of 10 years, 52 (9.4%) developed some form of atrio-ventricular block. Half of these (26) had total heart block, while of the other 26 patients, 12 had second-degree block and 14 first-degree block, that is, a P-R interval over 0.24 second. The infarct was posterior in 75% of the 52 cases, the proportion of posterior infarcts being even higher among those patients developing partial block. Heart block nearly always appeared within-one week of the infarction, with a maximum incidence on the 2nd and 3rd days.

In cases of total block the ventricular rate was often over 50 per minute and in some almost equalled the atrial rate. Of the 26 patients with total block, 18 died, death being mainly due to shock and not often to syncope accompanying Stokes—Adams attacks; the other 8 in this group recovered, the heart reverting to normal conduction. The prognosis for those with partial block was better, only 3 patients out of the 26 dying, while most of the remainder reverted to normal conduction.

J. A. Cosh

1139. Disorders of Atrio-ventricular Conduction in Recent Myocardial Infarction. II. Anatomical Study. (Les troubles de la conduction auriculo-ventriculaire dans l'infarctus myocardique récent. II. Étude anatomique) M. BLONDEAU, P. RIZZON, and J. LENÈGRE. Archives des maladies du cœur et des vaisseaux [Arch. Mal. Cœur] 54, 1104–1117, Oct. [received Dec.], 1961. 6 figs., 29 refs.

This anatomical and histological study of 26 hearts is based on 22 cases from the series reported above [see Abstract 1138], in 19 of which death followed infarction within a month, plus 4 more recent cases not included in the clinical study. Total block resulted from the infarct in 21 cases, and second or first degree block in 5. Cardiographically the infarcts were shown to be anterior in 12 and posterior in 14, and this paper describes the differences between these two types of lesion.

In all 14 cases of posterior infarction the lesion involved the upper and most posterior part of the septum, and often the adjoining part of the wall of the left ventricle as well. In 10 there was evidence of recent thrombosis of the right coronary artery, which was also the site of stenosis or old occlusion in the other 4. Of the 12 hearts with anterior infarcts, 11 showed lesions of the anterior part of the septum, sometimes with older lesions of its posterior part also, which in some cases involved the anterior wall of the left ventricle. The commonest

arterial changes associated with these infarcts were thrombosis (or earlier occlusion) of the anterior descending branch of the left coronary artery or of the right coronary artery, or in some of both together.

Histologically, in the cases of posterior infarction there was muscle necrosis at the very top of the septum, which approached but did not involve the interatrial septum. The A-V node and bundle of His were damaged in all cases, though never more than partially, being separated from the myocardial necrosis by a fibrous septum. In cases of anterior infarction a more variable picture was seen, the muscular lesion being not so high in the septum and more anterior; the A-V node and bundle of His were generally spared, but lower lesions of the bundle branches, particularly the right, were usual, and were often totally destructive. Posterior infarcts were thus associated with incomplete damage to the conducting system, which would explain the transitory nature of conduction defects in patients surviving the infarction. Anterior infarcts, however, were often associated with permanent damage to the right or (less often) the left bundle branches, but spared the A-V node.

J. A. Cosh

HEART FAILURE

1140. Effects of Isoproterenol on Cardiac Output and Renal Function in Congestive Heart Failure

H. SANDLER, H. T. DODGE, and H. V. MURDAUGH JR. American Heart Journal [Amer. Heart J.] 62, 643-651. Nov., 1961. 7 figs., 34 refs.

In normal subjects and in those with congestive cardiac failure the sympathomimetic amine isoprenaline (isoproterenol) increases cardiac contractility and lowers systemic vascular resistance, and in experimental animals it has been shown to possess a renal vasodilator action. In this study from the Veterans Administration Hospital and University of Washington School of Medicine, Seattle, and the Veterans Administration Hospital and Duke University School of Medicine, Durham, North Carolina, a comparison is made of the cardiovascular and renal effects of isoprenaline in 12 patients with congestive cardiac failure. Each patient was studied while fasting, though adequate hydration was ensured. Urirle was collected through an indwelling catheter, and blood levels of 10 to 20 mg. of inulin and 1 to 3 mg. of PAH per 100 ml. were maintained by means of a continuous intravenous infusion. After equilibration and after 3 15-minute control collection periods an intravenous infusion of isoprenaline was given at rates of 1 to 4 μ g. per minute, continuing for 2 or 3 15-minute collection periods. (In one patient this resulted in angina and a sinus tachycardia of 140 per minute.) Venous and arterial pressures and cardiac output were recorded, and vascular resistance was calculated from the difference between systemic arterial and venous pressures and systemic and renal blood flows.

In all subjects cardiac output and renal blood flow increased and mean peripheral venous pressure fell, but changes in the mean systemic arterial pressure were slight or inconsistent. The increase in cardiac output

was proportionately greater than the increase in renal blood flow in 9 cases, while renal blood flow increased in proportion to cardiac output in 2 and was more than the cardiac output in one. Lowering of systemic and renal vascular resistance occurred in all subjects, with a relatively greater fall in systemic resistance in 10. Effective renal plasma flow (clearance of PAH×1/0·9) invariably increased, but the effects of isoprenaline on glomerular filtration were slight and variable. The changes in urine flow were also variable, and while there was a relative increase in 9 subjects, the changes in the flow of urine for the group were not statistically significant.

The concentration of sodium in the urine was determined in 8 subjects and an increase in sodium excretion, which was not statistically significant, was demonstrated in 7. When the amounts of sodium filtered per minute, however, were related to those excreted per minute $(C_{Na}:C_{IN})$ a significant increase in the percentage of filtered sodium which was excreted was found for the group as a whole.

Eirian Williams

1141. Bendroflumethiazide Diuresis in Congestive Heart

G. A. PORTER and N. A. DAVID. Journal of New Drugs [J. New Drugs] 1, 150-156, July-Aug. [received Nov.], 1961. 1 fig., 23 refs.

A study of the diuretic action of a new benzothiadiazine derivative, bendroflumethiazide, in 21 patients with congestive cardiac failure and 2 with ascites due to cirrhosis is reported from the University of Oregon Medical School and Hospitals, Portland, Oregon. The ages of the patients (18 male and 5 female) ranged from 36 to 86 years and the cardiac conditions present included hypertensive, arteriosclerotic, rheumatic, luetic, and congenital heart disease. None of the patients had received recent diuretic therapy. After a 3-day stabilization period with rest in bed, digitalis, 1 g, of sodium daily, and unrestricted water, a 24-hour specimen of urine was taken for control measurements. Bendroflumethiazide was given by mouth in a dosage of 5 to 10 mg, daily before breakfast for 3 to 29 days. The diuretic response was assessed from changes in body weight; urinary volume, and urinary excretion of sodium, potassium, and chloride. Periodically blood pressure and the blood count were recorded and the levels of serum electrolytes and blood urea nitrogen were determined.

Over the whole series the average daily changes in the parameters assessed included increases in weight loss of 1.5 lb. (0.68 kg.), in urinary volume of 705 ml. ±261 ml. (95% confidence limits), and in sodium excretion of 60.8 mEq. ±23.9 mEq. paralleled closely by an increase in chloride excretion of 64.1 mEq. ±27.6 mEq.; the increase in potassium loss was only 9.7 mEq. ±13.3 mEq. No significant changes were observed in the serum electrolyte values. There was a fall in blood pressure in hypertensive but not in normotensive patients. Hyponatraemic symptoms developed in only one patient, while 3 others had minor side-effects attributable to the drug.

The authors conclude that bendroflumethiazide in a dosage of 5 mg, daily is a prompt and effective drug in the treatment of congestive cardiac failure, is more

efficacious than hydroflumethiazide, and has a therapeutic action equal to that of hydrochlorothiazide.

Gerald Sandler

1142. Treatment of Intractable Heart Failure in the Presence of Complete Atrioventricular Heart Block by the Use of the Internal Cardiac Pacemaker: Report of Two Cases

O. F. MULLER and S. BELLET. New England Journal of Medicine [New Engl. J. Med.] 265, 768-772, Oct. 19, 1961. 3 figs., 16 refs.

The successful treatment of 2 cases of intractable cardiac failure associated with complete atrioventricular block due to arteriosclerotic heart disease is described in this paper from the Philadelphia General Hospital, Pennsylvania. Both patients had failed to respond to diuretics, digitalis, thoracentesis, and rest in bed, and the heart rate remained between 20 and 30 beats a minute in spite of administration of sympathomimetic drugs, corticosteroids, and molar sodium lactate. There was a consequent low cardiac output with a fixed stroke output. Minute transistorized cardiac catheter electrodes were introduced through the external jugular vein into the cavity of the right ventricle and connected to a pacemaker. The ventricular rate was increased by electric stimulation to 50 to 65 beats a minute, above which cardiac output fell sharply. Up to this point there was a significant increase in the cardiac output in the one patient in whom this was measured, with a marked clinical improvement in both. One of the patients died suddenly after 7 weeks from a fresh myocardial infarction: the other was fit enough to be discharged with the elec-trode still in place.

One further case is briefly mentioned, that of a woman, aged 67 years, who underwent nephrectomy after the heart rate had been increased from 28 to 58 beats a minute and cardiac output by 60%. The authors advocate the use of an artificial pacemaker in desperately ill patients with complete heart block and intractable cardiac failure if all available medical measures have failed.

J. Warwick Buckler

1143. Reticulocytosis and Hypoxemia as Prognostic Signs in Congestive Heart Fallure

J. THOMAS, O. MICHAEL, and C. W. EWELL. Circulation [Circulation] 24, 1151-1153, Nov., 1961. 1 fig., 4 refs.

Fifteen patients with severe congestive heart failure were studied at the George W. Hubbard Hospital of Meharry Medical College, Nashville, Tennessee, to determine the prognostic significance of the appearance of immature erythrocytes in the peripheral blood and the role of hypoxaemia as an unfavourable event. In all the patients except one the arterial oxygen saturation was reduced, and the average of these findings indicated a reciprocal relationship between the degrees of hypoxaemia and reticulosis. In all of 5 patients who died within one month of admission to hospital the reticulocyte count was consistently greater than 3% (average 4%) and 2 of these patients had nucleated erythrocytes in the peripheral blood. On the other hand in all of 10

patients who improved and survived the reticulocyte count was less than 2.2% (average 1.5%).

There was no demonstrable clinical difference between the patients who died and those who survived; in fact some of the former had a better clinical prognosis than some of the latter. The findings therefore suggest that a rise in the reticulocyte count in patients with congestive heart failure indicates an unfavourable prognosis and is a more useful index than the nucleated crythrocyte count.

P. T. O'Farrell

BLOOD VESSELS

1144. Surgical Correction of Coarctation of the Aorta by an "Isthmusplastic" Operation

K. VOSSSCHULTE. Thorax [Thorax] 16, 338-345, Dec., 1961. 5 figs., 13 refs.

The author of this paper from the University Surgical Clinic, Giessen/Lahn, Germany, describes 14 patients in whom a plastic procedure on the stenosed segment of the aortic wall has produced a haemodynamically satisfactory operative result. In the "direct isthmusplastic" operation the aorta is incised longitudinally immediately above and below the coarctation and then repaired transversely with interrupted everting sutures. In the "indirect isthmusplastic" operation (indicated in cases in which a long segment of the aorta is stenosed) a longitudinal incision, carried proximally if necessary into, the subclavian artery, is made and then subsequently closed with a "teflon" patch of appropriate size. The advantages claimed for the isthmusplastic procedure are: (1) quicker operation as a result of more limited exposure of the aorta; (2) no restenosis due to scar shrinkage, as follows a circular suture; (3) good exposure of site of arterial suture; and (4) applicability to all types of coarctation, including those cases in which the aortic wall is atheromatous. Three illustrative case histories are given. R. L. Hurt

1145. Genesis and Actiology of the Crossing Phenomenon and Its Significance in the Diagnosis of Retinal Vascular Diseases. (Die Genese und Atiologie des Kreuzungsphänomens und seine Bedeutung für die Diagnostik von Netzhautgefässerkrankungen)

R. SETTZ. Klinische Monatsblätter für Augenheilkunde [Klin. Mbl. Augenheilk.] 139, 491-512, Nov., 1961. 22 figs., 31 refs.

On the basis of 100 ophthalmoscopic observations made at the University Eye Clinic, Tübingen, of the crossing phenomenon in the living subject, followed by serial histological examination of the parts observed, the author discusses the genesis of the phenomenon and its diagnostic significance, on which much stress has been laid. The crossing phenomenon has been regarded as pathognomonic for certain retinal vascular diseases and has usually been explained as resulting from compression of the underlying vein by the thickened artery. This compression of the vein, however, has been denied by von Sallmann, and the present author agrees with him.

The basic disease, whether it be arteriosclerosis, hypertension, or Kimmelstiel's disease, causes certain changes in the vessel wall, such as sclerosis, fibrosis, or hyalinosis. This may occasionally cause narrowing of the lumen, but the relationship between the artery and vein remains the same as in the normal eve. In none of the 74 minutely studied cases could compression of the undercrossing vein be demonstrated in the histological picture. The phenomenon is always caused by thickening of the vessel wall and of the common adventitiae and gliae cover causing the blood column to appear thinner. There is no real stasis at the crossing proximally, as the author shows in preparations derived from cases of different retinal vascular diseases (among them one of melanoma of the choroid), and the calibre of the vein is the same on both sides of the crossing. When there is real stasis, as demonstrated in a case of papilloedema with prethrombosis and fresh thrombosis of the central retinal vein respectively, the calibre of the vein peripheral to the obstacle (and crossing) is much wider than centrally to it. Finally, by schematic representations the different crossing phenomena and their histological equivalents are discussed. In the author's view the crossing phenomenon is important only as a pointer to some change in the vascular and perivascular walls and gives no indication of the degree of hypertensive disease or its prognosis. L. Wittels -

1146. Effect of Tolbutamide on Peripheral Arterial Discase

S. D. CLARKE and F. D. NAYLOR. Lancet [Lancet] 2, 1327-1328, Dec. 16, 1961. 1 fig., 3 refs.

Singh and Brara (Lancet, 1960, 2, 625; Abstr. Wld Med., 1961, 29, 227) obtained dramatic relief of pain with tolbutamide in 34 of 36 cases of thromboangiitis obliterans. The chief symptom in one-third of these cases was said to be intermittent claudication. Tolbutamide has also been found to relieve the pain of cardiac ischaemia. In the present paper from the University of Sheffield the authors describe a double-blind trial designed to determine the effect of tolbutamide on peripheral arterial disease due to atheroma, intermittent claudication being the criterion for the selection of cases. In assessing the effect of the drug reliance was not placed on subjective changes but on the results of clinical examination, ergometry, and oscillometry and on skin temperatures.

The drug was given in a dosage of 0.5 g. 3 times a day to 32 patients who were seen at monthly intervals. The effect of tolbutamide was essentially similar to that of the placebo tablets tried, and the authors therefore consider that the drug is without value in this condition.

Leon Gillis

1147. The Risk of Interrupting Long-term Anticoagulant Treatment: a Rebound Hypercoagulable State following Hemorrhage

H. S. Sise, C.B. Moschos, J. Gautener, and R. Becker. Circulation [Circulation] 24, 1137-1142, Nov., 1961. 1 fig., 12 refs.

From a series of 310 patients on long-term anticoagulant treatment for various conditions 136 instances were collected in which treatment was interrupted. This was

because of bleeding in 45 instances, for permanent reasons in 53 instances, and for temporary reasons in 38 instances.

Rebound thromboembolic complications were observed significantly more frequently in those who stopped treatment for bleeding. The cause of the rebound effect could not be ascribed to vitamin K₁ administration, transfusions, or overt ischemic effects from blood loss although the latter might have been contributory to a small extent. The observations suggested a hypercoagulable state induced directly in some obscure way as a result of the bleeding.

Interruption of treatment for reasons other than bleeding was not associated with early complications. The risk of interruption of treatment for short periods was relatively small (three nonfatal complications in 38 instances). In those who stopped permanently, complications were most often seen after 2 months.—[Authors' summary.]

SYSTEMIC CIRCULATORY DISORDERS

1148. Effect of Thiazides on Carbohydrate Metabolism in Patients with Hypertension

A. P. Shapiro, T. G. Benedek, and J. L. Small. New England Journal of Medicine [New Engl. J. Med.] 265, 1028–1033, Nov. 23, 1961. 3 figs., 19 refs.

The diabetogenic effect of the thiazide group of drugs has been noted by several workers and the authors of this paper from the University of Pittsburgh School of Medicine, Pennsylvania, state that they observed it in 5 elderly patients in whom symptomatic diabetes mellitus developed while receiving chlorothiazide as an antihypertensive agent. In these patients the drug was discontinued and carbohydrate tolerance improved rapidly, although 4 of them required insulin temporarily.

In a systematic investigation of this diabetogenic effect the authors carried out oral glucose tolerance tests (1.75 g. of glucose per kg. body weight) in two groups each of 15 patients before and during administration of chlorothiazide in a dosage of 1 to 1.5 g. daily. The first group were hypertensive and 7 of them had a family history of diabetes mellitus. All 15 had slight impairment of carbohydrate tolerance with a peak blood sugar level of 180 mg. per 100 ml. or more at one hour after glucose loading, and were designated, "potential diabetics". The second control group had normal glucose tolerance curves and no family history of diabetes; 10 of them were hypertensive. In the potential diabetics during chlorothiazide therapy there was an average rise in the blood sugar level of 26, 39, 41, and 34 mg. per 100 ml. at zero time and at 1, 2, and 3 hours respectively after glucose loading, compared with the previous blood sugar curves. In the nondiabetic group chlorothiazide produced no significant change in glucose tolerance. The two groups showed typical nondiabetic and diabetic responses to intravenous injection of 1 g. of tolbutamide. In the non-diabetic group the blood sugar level fell to 55.5% of the resting level at 30 minutes with subsequent rise, whereas in the diabetic group the fall at 30 minutes was

to 83.5% of the resting level and the level had fallen further at one hour. The tolbutamide response tests were repeated in both groups during chlorothiazide therapy. The non-diabetics showed no significant change in blood sugar levels, but the shape of the curve changed slightly towards a diabetic type. In the diabetic group the shape of the curve was unaltered, but the blood sugar level in all was significantly higher. In 5 healthy medical students chlorothiazide administration produced no change in response to tolbutamide.

K. G. Lowe

1149. Effect of Thiazide Diuretics on Plasma Volume, Body Electrolytes, and Excretion of Aldosterone in Hypertension

R. W. Gifford Jr., V. R. MATTOX, A. L. ORVIS, D. A. Sones, and J. W. Rosevear. *Circulation [Circulation]* 24, 1197–1205, Nov., 1961. 4 figs., 23 refs.

The hypotensive effect of three thiazide diuretics—chlorothiazide, hydrochlorothiazide, and trichlormethiazide—was studied at the Mayo Clinic in 28 patients with sustained diastolic hypertension of mild to moderate severity; none had congestive cardiac failure, detectable oedema, or azotaemia and there were no dietary restrictions or supplements.

During the first week of treatment there was a statistically significant reduction (mean 8.8%) in plasma volume, which was measured by the Congo red technique. With continued treatment, however, the plasma volume gradually returned to normal or toward it. A correlation was observed between the initial reduction in plasma volume and the mean fall in blood pressure. The diuretics produced an increase in urinary sodium excretion, but no change in serum sodium levels or exchangeable body sodium values. A few potassium estimations suggested a slight reduction in the serum potassium level early in the course of diuretic therapy. Exchangeable body potassium content was reduced initially, but later increased beyond the control values. Determination of urinary aldosterone excretion 16 times in 9 patients showed that almost all the results were within normal limits and did not vary significantly from pre-treatment levels. The authors have to conclude that the mechanism of the hypotensive action of thiazide derivatives has not yet been elucidated. K. G. Lowe

1150. Clinical Observations on the Retina in Essential Hypertension. Ophthalmodynamometry and Measurement of the Calibre of the Retinal Vessels. (Klinische Beobachtungen an der Netzhaut bei essentieller Hypertonie. Ophthalmodynamometrie und Kalibermessung der Netzhautgefässe)

M. MIKUNI, N. SHIRAKASHI, and T. NAHASHIZUKA. Klinische Monatsblätter für Augenheilkunde [Klin. Mbl. Augenheilk.] 139, 465–475, Nov., 1961. 13 refs.

In 73 healthy subjects and in 80 patients with essential hypertension (who had been classified according to the Keith-Wagener scale into Stage I 35, Stage II 36, Stage III 5, and Stage IV 4) the calibre of the retinal vessels and ophthalmodynamometry of the retinal blood pressure were measured at the University Eye Clinic, Niigata, Japan, with the following results. The mean arterial

calibre showed statistically significant differences between the normal subjects and patients in Stage I, between Stages I and II, and between Stages II and III, but the difference in calibre between Stages III and IV was not significant. In the veins significant differences in calibre were found between Stages I and II and III, but not between normal and Stage I or between Stages III and IV. In regard to the ratio of arteries to veins, a significant difference was seen only between Stages II and III. In other words, as hypertensive disease progresses the arteries and veins become progressively narrower, but not beyond Stage III, which marks the beginning of malignant hypertension.

There was a significant difference in the mean arterial retinal pressure between normal and Stage I, between Stages I and II, and between Stages II and III, but not between Stages III and IV. In the venous pressure a statistically significant difference was found only between Stages II and III. Papilloedema was shown to cause a higher mean value. The ratio between the retinal arterial and systemic blood pressures presented a statistically significant difference similar to that between the retinal pressures themselves. The numerical expression of malignant hypertension would be a decrease to below 70% in the calibre ratio between arteries and veins and an increase to above 70% in the blood-pressure ratio.

L. Wittels

1151. Some Principles of Hypotensive Therapy Considered in Relationship to the Pathogenesis of Essential Hypertension

F. H. SMIRK. American Journal of Cardiology [Amer. J. Cardiol.] 9, 90-99, Jan., 1962. 2 figs., 28 refs.

1152. Sympathetic Denervation of the Upper Extremities in Raynaud's Disease and Secondary Raynaud's Phenomenon. [In English]

B. Fretheim. Acta chirurgica Scandinavica [Acta chir. scand.] 122, 361-370, Nov., 1961. 5 figs., 11 refs.

At Rikshospitalet, Oslo, thoracic sympathectomy was carried out on 26 patients suffering from Raynaud's phenomenon, bilaterally in 20, Smithwick's technique being used. Of these patients, 23 had primary Raynaud's disease and 3 had secondary Raynaud's phenomena. All the patients had been treated medically for an extended period before the operation. The only clear-cut indication for sympathectomy was gangrene of the finger tips, which, however, occurred in only 2 patients. The average age of the patients at the time of operation was 34 years, and the follow-up period ranged from 6 months to 10 years.

In the author's view preganglionic sympathectomy of this type achieves good results in Raynaud's disease. It increases the skin temperature level in the hands, which is gradually reduced to approximately normal during the first 5 years after surgery. Raynaud's phenomenon does not disappear completely, but patients who still experience symptoms are less troubled by them, the attacks being less severe. No complication of any severity was noted in the present series and there were no deaths.

I. McLean Baird

Clinical Haematology

1153. Folic Acid Metabolites in Whole Blood and Serum in Anemia of Pregnancy

G. IZAK, M. RACHMILEWITZ, A. SADOVSKY, B. BERCOVICI, J. ARONOVITCH, and N. GROSSOWICZ. American Journal of Clinical Nutrition [Amer. J. clin. Nutr.] 9, 473–477, July-Aug.; 1961. 1 fig., 23 refs.

The authors have determined the folic acid and folinic acid levels in whole blood and serum of pregnant women aged 16 to 42 years delivered at the Hebrew University Hospital, Jerusalem: Three microbiological assay methods were used simultaneously, the organisms being Lactobacillus casei, Streptococcus faecalis, and Paediococcus cerevisiae. Among the 1,500 women examined, 420 (28%) were found to be anaemic at the time of delivery (that is, haemoglobin levels below 10 g. per 100 ml.). Significantly low total folic acid values were found in whole blood as well as in serum in about half the patients and these low values were frequently associated with low serum levels of iron and/or vitamin B₁₂. There was, however, no correlation between the low values and the type of the anaemia. A characteristic hyperchromic macrocytic anaemia was found in only 7 patients, the anaemia in the majority (56%) being dimorphic.

Since examination of foetal blood showed that it contained about eight times more folinic acid than did the corresponding maternal blood, whereas the folic acid content was only twice as great, the authors suggest that conjugated folic acid may be mobilized from the maternal erythrocytes and find its way across the placenta to the foetus, where it is found mainly in its metabolically active forms. Large foetal demand is therefore mainly responsible for a relative folic acid deficiency in the mother and thus contributes to the development of the anaemia of pregnancy.

Janet Vaughan

1154. The Plasma Clearance of Injected Doses of Folic Acid as an Index of Folic Acid Deficiency

J. METZ, K. STEVENS, S. KRAWITZ, and V. BRANDT. Journal of Clinical Pathology [J. clin. Path.] 14, 622-625, Nov., 1961. 19 refs.

The authors have studied at the South African Institute for Medical Research, Johannesburg, the plasma clearance of injected doses of folic acid as an index of folic acid deficiency in normal white subjects, patients with megaloblastic anaemia, healthy Bantu males and females, and patients with scurvy. The clearance of injected folic acid is abnormally rapid in megaloblastic anaemia due both to vitamin-B₁₂ deficiency and folic acid deficiency; it is also rapid in scurvy. The authors suggest that this may be due to an associated dietary deficiency of folic acid. They also found a rapid clearance of injected folic acid in some Bantu women who were not anaemic, but the clearance in Bantu males followed the same pattern as in healthy white subjects. They suggest that the

test is sufficiently sensitive to detect subclinical deficiency of folic acid in Bantu women before the development of frank anaemia. Janet Vaughan

1155. Paroxysmal Nocturnal Haemoglobinuria: Variation in Clinical Severity and Association with Bonemarrow Hypoplasia

J. V. DACIE and S. M. LEWIS. British Journal of Haematology [Brit. J. Haemat.] 7, 442-457, Oct., 1961. 8 figs., 32 refs.

The extremely chronic and variable clinical course of paroxysmal nocturnal haemoglobinuria (P.N.H.) is discussed and 3 cases seen at Hammersmith Hospital, London, are described. It is shown that the defect may, though rarely, disappear completely. One patient had the disease in its most severe form but was kept alive for 11 years by the transfusion of about 300 bottles of blood, which were estimated to contain approximately 60 g. of iron. In spite of this only renal siderosis was found at necropsy. The absence of the picture of haemochromatosis was presumably due to the loss of iron in the urine; this was found during several periods to be about 10 mg. a day, an amount which would account for most of the iron deficit.

The authors discuss the difficulties of diagnosis, the frequency of thrombocytopenia and leucopenia in cases of P.N.H., and the observation that the reticulocyte response to haemolysis often seems deficient. Marrow hypoplasia and ineffective myelopoiesis quite often occur and the haemolytic element may be dormant. They cite 2 patients (brothers) described in the literature who had P.N.H. but in whom the initial diagnosis was Fanconi's familial aplastic anaemia. The P.N.H. defect is, however, very rarely found in patients with aplastic anaemia. Discussing the value of splenectomy in P.N.H. the authors note that many workers consider the operation to be ineffective and dangerous. However, there are also reports of clinical improvement following this operation, with reduction in transfusion requirements.

R. B. Thompson

1156. Failure of *in-vivo* Inhibition of Acetylcholinesterase to Affect Erythrocyte Life-span: the Significance of the Enzyme Defect in Paroxysmal Nocturnal Haemoglobinuria J. Metz, K. Stevens, N. J. van Rensburg, and D. Hart. *British Journal of Haematology* [Brit. J. Haemat.] 7, 458–463, Oct., 1961. 2 figs., 14 refs.

A deficiency of erythrocyte cholinesterase has been demonstrated in paroxysmal nocturnal haemoglobinuria (P.N.H.), the degree of which seems to be correlated with the activity of the haemolytic process. In an investigation carried out under the auspices of the South African Institute for Medical Research, Johannesburg, an attempt was made in 5 haematologically normal subjects to inhibit erythrocyte cholinesterase by administration orally of

5 mg. daily of octamethylpyrophosphoramide (OMPA). Erythrocytes were labelled with radioactive chromium in 3 subjects 6 days before the OMPA was given and in 2 subjects after 21 days' administration of the drug. The survival of the labelled cells was then studied. Before and after administration of OMPA observations were made of the effect of acidification of a 50% suspension of washed erythrocytes and the effect on the erythrocytes of a serum containing a high titre of cold antibody; a Crosby test was also carried out. In none of the subjects could any significant shortening of erythrocyte life-span be demonstrated; none of the features of P.N.H. developed and there were no side-effects.

It is pointed out that these results may not necessarily mean that acetylcholinesterase deficiency is not of importance, for the negative findings may be due to inadequate enzyme inhibition.

R. B. Thompson

1157. Idiopathic Thrombocytopenic Purpura: Treatment in Adults

W. L. BUNTING, J. M. KIELY, and D. C. CAMPBELL. Archives of Internal Medicine [Arch. Intern. Med.] 108, 733-738, Nov., 1961. 10 refs.

At the Mayo Clinic during the 5-year period 1954 to 1958 idiopathic thrombocytopenic purpura (I.T.P.) was diagnosed in 100 patients aged 15 years or older, and in this paper the outcome in 87 who were available for follow-up is reported. In 22 of the patients the illness was acute—that is, symptoms had been present for less than 6 months—and in 65 it was chronic.

Adrenal steroids were given to 16 of the patients with acute I.T.P.; 4 responded satisfactorily, but the remaining 12 failed to benefit and were therefore subjected to splenectomy. Cure was achieved in 10, only 2 of whom were still receiving steroids, while 2 continued to have mild or intermittent purpura. Splenectomy was eventually performed on 18 of the 22 patients with acute I.T.P. with success in 14, including 12 who had not received steroids or from whom steroids had been withdrawn, the satisfactory result being unequivocably attributed to the operation.

Of the 65 patients with chronic I.T.P., 13 received no treatment, purpura in 12 of them being mild with slight or moderate thrombocytopenia. Steroids were given to 26; but only 2 obtained full remission. Of the 24 who did not respond satisfactorily to steroids, 6 received no other form of treatment and 18 underwent splenectomy. A remission was obtained in 6, while 2 others responded when steroids were again given postoperatively; in the remaining 10 patients splenectomy was unsuccessful. Altogether 44 patients with chronic I.T.P. eventually underwent splenectomy, 23 successfully, including 17 who had had no previous steroid therapy. Of the 21 in whom splenectomy failed, 9 did not receive steroids either before or after operation; in 3 of these the platelet count became normal 4 or more years after operation and in 6 thrombocytopenia was minimal, requiring no specific treatment. Two patients with chronic I.T.P., both of whom had received steroids, died, one from haemorrhage 15 days after splenectomy and the other from a transfusion reaction during relapse following splenectomy.

The authors conclude from these findings that while it may be preferable in acute I.T.P. initially to try the effect of steroids, in chronic I.T.P. the treatment of choice is splenectomy.

Eirlan Williams

NEOPLASTIC DISEASES

1158. Radio-isotope Investigations in Primary Myeloid Metaplasia

A. J. BOWDLER. Journal of Clinical Pathology [J. clin. Path.] 14, 595-602, Nov., 1961. 3 figs., 36 refs.

At University College Hospital, London, the author has investigated 14 cases of "primary myeloid metaplasia", using radioactive chromium and radioactive iron to assess erythrocyte survival, iron utilization, and the patterns of the surface counts over various organs. The results add little to our understanding of the pathogenesis of myeloid metaplasia, but suggest that such investigations may be useful in the investigation and management of the varied group of conditions in which such metaplasia is found. The anaemia of primary myeloid metaplasia appears to depend in the first place on impaired marrow activity and only later in some cases on accelerated erythrocyte destruction due to both intraand extra-corpuscular factors. The isotope techniques employed may indicate that active haemolysis is taking place, in which case removal of the spleen may be indicated. On the other hand, if it is apparent that active haematopoiesis is taking place in the spleen and is accompanied by marked failure of haematopoiesis in the marrow, it is unwise to perform splenectomy. In patients in whom biopsy of the liver, spleen, or marrow is inadvisable owing to a haemorrhagic tendency the author suggests that isotope techniques may offer an alternative method of diagnosis and in this way also be of value. Janet Vaughan

1159. A Method for Evaluation of Disease and Treatment of Chronic Leukemia

S. W. Ross, E. J. MACDONALD, P. DAVIS, J. HAMMAR-STEN, and W. C. LEVIN. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 559-579, Oct., 1961. 8 figs., 11 refs.

In these studies, which were carried out under the auspices of the (U.S.) Southwest Cancer Chemotherapy Study Group, a system of scoring was devised to enable the severity of the disease in patients with chronic hymphatic leukaemia and chronic myeloid leukaemia to be expressed. In this system 11 clinical or haematological features were assessed, these including activity status, degree of anaemia, need for blood transfusion, total leucocyte count, degree of splenomegaly and hepatomegaly in both diseases, as well as the degree of lymphadenopathy in chronic lymphatic leukaemia, and the percentage of blast cells in chronic myeloid leukaemia. Each of these features was scored according to a scaled measure of severity, so that in any one patient the higher the total score, the greater the deviation from normal.

For the evaluation of the method 91 patients with chronic lymphatic leukaemia and 45 with chronic mye-

loid leukaemia were observed by members of the group at intervals of 2 or 4 weeks over a period of 18 months and their scores adjusted in accordance with the findings. On this basis the patients could be divided into two groups, those with initial scores of 10 or less and those with initial scores of 11 or more. In both diseases the patients with the lower scores tended to have higher initial haemoglobin levels and to be capable of more unrestricted activity. In respect of some other features the two groups did not differ significantly, namely, in chronic lymphatic leukaemia as regards degree of splenomegaly or hepatomegaly, and in chronic myeloid leukaemia as regards total leucocyte count, platelet count, and degree of hepatomegaly. The authors are satisfied that the score generally reflects the sum of the effects of the features of the diseases. In both diseases the mean initial score was significantly lower than the mean final score, and the length of time a patient maintained the same score was inversely related to the level of the score.

Finally, in order to test the validity of the scoring system in relation to the natural history of the two diseases patients were assigned to one of 4 groups, those having the lowest initial score being placed in Group 1. Initial scores and scores after 12 months were then compared. It was found that of the patients with chronic lymphatic leukaemia only those placed initially in Group 4 still differed significantly from the other groups and that while the scores for Group 1 differed significantly from those for Group 3, those for Groups 1 and 2 and Groups 2 and 3 did not. In chronic myeloid leukaemia the only significant difference in scores which persisted after 12 months was that between Group 4 and all the others. Because of this finding the authors suggest that the scoring system may require some modification. By similar comparisons after 12 months they found that in chronic lymphatic leukaemia the mortality in Group 1 was 5% and in Group 4 60%, while in chronic myeloid leukaemia the rates were 2% and 100% respectively. Because of these findings they suggest that patients who on the basis of initial scores are placed in Groups 2 and 3 are those most suitable for inclusion in therapeutic trials since they are the most responsive to treatment.

A. G. Baikie

1160. Chemotherapy and Remission in Acute Leukaemia in Children

J. H. COLEBATCH. Medical Journal of Australia [Med. J. Aust.] 2, 624-628, Oct. 14, 1961. 2 figs., 3 refs.

Experience of chemotherapy in acute leukaemia in childhood is described with reference to the results obtained in 105 patients seen at the Royal Children's Hospital, Melbourne, over a recent 2½-year period. The ages of the children at the onset of symptoms ranged from 5 months to 13 years, with a peak at 3 years. The series included 37 definite and 27 probable cases of acute lymphatic leukaemia, 6 definite and 24 probable cases of acute myeloid leukaemia, and 8 cases of acute leukaemia which could not be designated as of the myeloid or lymphatic type. In addition there were 2 patients with chronic myeloid leukaemia and one with "acute monocytic anaemia".

From the start of the series in January, 1959, each child received 6-mercaptopurine. Until July, 1959, prednisolone was also given. For the last 20 months of the trial chemotherapy was begun in all new cases with 6-mercaptopurine in a dosage of 5 mg. per kg. body weight daily for 4 days, followed by 2.5 mg. per kg. indefinitely. When neutropenia or thrombocytopenia was present prednisolone was given initially in a dosage of 2.5 to 3 mg. per kg. daily, the dose being reduced as soon as the neutrophil or platelet count started to rise. Administration of 6-mercaptopurine was discontinued when signs of a relapse appeared. At this stage an antifolic-acid drug was given. In the last 6 months a cyclophosphamide of nitrogen was tried, but was found to be inferior to the 3 drugs already tried.

The results with this regimen in 50 patients are tabulated. Complete remission was obtained in 32 out of 35 cases of acute lymphatic leukaemia and in 7 out of 14 of acute myeloid leukaemia, the remission occurring within a median period of 5 weeks. It is concluded that with this treatment 50% of children with leukaemia will survive for at least 14 months and 10% for at least 2 years.

A. W. H. Foxell

1161. Study of Chromosomes in Human Leukaemia by a Direct Method

M. A. KINLOUGH and H. N. ROBSON. *British Medical Journal [Brit. med. J.*] 2, 1052–1055, Oct. 21, 1961. 3 figs., 15 refs.

This paper from the University of Adelaide, South Australia, reports the results of direct chromosome studies on cells from the bone marrow or peripheral blood in 16 cases of leukaemia; neither of the two methods used to obtain dividing cells for examination involve culturing. In some cases bone marrow was aspirated one hour after the intravenous administration of colchicine, as described by Kinlough et al. (Nature (Lond.), 1961, 189, 420). However, the administration of colchicine was later found to be unnecessary, since when EDTA (dipotassium salt) was used as anticoagulant this substance exerted a colchicine-like effect on both bone marrow cells and peripheral blood leucocytes (Kinlough and Robson, Nature (Lond.), 1961, 189, 684).

Of 8 cases of acute leukaemia, chromosome abnormality was found in 2. The modal chromosome number in both cases was 47 and in both the extra chromosome was of the size of the pairs 13-15. No chromosome abnormality was found in 4 cases of chronic lymphatic leukaemia. The Philadelphia chromosome (Ph¹) was seen in 2 of 4 cases of chronic myeloid leukaemia. The authors mention that the cases in which the Ph¹ chromosome was not seen were studied early in the series when the quality of the preparations hardly allowed a decision to be made on the presence or absence of the abnormality. The advantages of direct methods of chromosome study, without preliminary culture, are discussed.

[It is regrettable that no information is given as to whether a result in a particular patient was obtained with blood or bone-marrow cells. Nor are we told in how many cases studies were attempted to yield these results.]

A. G. Balkie

Respiratory System

1162. Corticosteroids as a Means of Differential Diagnosis in Doubtful Disease of the Lungs. (Die Corticosteroide als differentialdiagnostisches Hilfsmittel bei unklaren Erkrankungen der Lungen)

G. DE CAMP. Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung [Beitr. Klin. Tuberk.] 124, 503–514, 1961. 10 figs., 4 refs.

This paper comes from the Havelhöhe Clinic for Lung Diseases, Berlin-Kladow, where during the past 6 years over 1,300 patients have been treated with steroids, mostly for tuberculosis, but 300 patients had malignant disease, particularly bronchial carcinoma. Since it was found that prednisone had a good effect in cases of pneumonia and lung abscess, it occurred to the author that steroids could be used to help to establish the diagnosis in those cases in which it remained doubtful, despite full clinical examination supported by chest radiography. He describes 5 illustrative cases occurring in 3 female and 2 male patients ranging in age from 17 to 60 years.

The first patient was a 60-year-old woman whose chest radiograph in December, 1960, showed a left hilar shadow suggestive of carcinoma. Prednisone and penicillin were given [dose unstated]; by February, 1961, the chest was clear and bronchoscopy showed a normal picture. The second patient, a man also aged 60, had been ill for 3 months. In April, 1959, the chest radiograph showed a left-sided cavity with a fluid level and pneumococci were cultured from the sputum. After treatment with 255 mg, of prednisone and erythromycin [dose not stated] the chest was clear one month later and the results of bronchography and bronchoscopy were normal. In the third case a 28-year-old woman had had fever and cough for 2 weeks. X-ray examination of the chest showed a left subapical shadow suggestive of tuberculosis. The sputum, however, was negative for tubercle bacilli and the tuberculin test was positive to 10 t.u. Prednisone (380 mg. in all) and chemotherapy were given and one month later the chest was clear. The remaining 2 cases showed similar features and similar

The author concludes that a trial of combined steroids and chemotherapy is valuable in the differential diagnosis of difficult cases, especially in those cases of pneumonia and lung abscess which may be confused with tuberculosis or carcinoma. The rapid response to these drugs is the essential factor in excluding the more serious disease. Altogether, 24 cases of carcinoma and 10 of tuberculosis that could not be diagnosed by routine methods were discovered in this way.

[Although the anti-inflammatory action of steroids is well known, their use in infections other than meningococcal is not to be advised as a routine. In the abstracter's view the author of this paper has not made out a valid case for the use of steroids, and he seems to have discounted the valuable effect of penicillin alone in the treatment of the pneumonias.]

I. M. Librach

1163. Increased Oestrogen Excretion in Hypertrophic Pulmonary Osteoarthropathy

J. GINSBURG and J. B. BROWN. Lancet [Lancet] 2, 1274-1276, Dec. 9, 1961. 1 fig., 15 refs.

In this study reported from St. Thomas's Hospital, London, and the M.R.C. Endocrinological Research Unit, University of Edinburgh, the urinary excretion of oestrogen in 11 patients with pulmonary osteoarthropathy (10 with carcinoma of the lung) was compared with that in a control group consisting of 7 patients with carcinoma of the lung but without arthropathy (of whom 3 had digital clubbing), 5 with clubbing or gynaecomastia associated with other disease, and 24 healthy men. In . the patients with pulmonary arthropathy the mean excretion of oestrogens was more than twice that in the controls: 8 of the 11 excreted more oestriol than normal, 3 more oestrone, 6 more oestradiol, and 7 more total oestrogens; the increase was greatest in respect of the oestriol fraction. Between 4 and 8 weeks after removal of the primary pulmonary tumour in 6 of the cases the oestrogen excretion had fallen to less than half the preoperative levels, and in all it had returned to normal.

The cause of this increased excretion of oestrogen is not clear. It could not be due to the tumour itself, as in those patients with tumour but without arthropathy oestrogen excretion was normal and in one of the 6 operated cases the level of excretion increased considerably in the first week after removal of the tumour, nor was it associated with clubbing or with gynaecomastia. Further, the conjugation and inactivation of oestrogens were apparently not impaired, since it was found that the recovery of injected oestradiol in the form of the three urinary oestrogens was normal; likewise in the patients studied there was no clinical or biochemical evidence of adrenal or hepatic abnormality.

A. Gordon Beckett

1164. Clinical Usefulness of the Single-breath Pulmonary Diffusing Capacity Test

B. Burrows, J. E. Kasik, A. H. Niden, and W. R. Barclay. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 789-806, Dec., 1961. 6 figs., 36 refs.

This report is based on 555 determinations of the single-breath pulmonary diffusing capacity (D_L) performed as a clinical service at the University of Chicago clinics. From the results in 135 subjects in this group who had no significant cardiopulmonary disease regression formulae were obtained as follows: for men $D_L=15\cdot5\times$ body surface area $-0\cdot238\times$ age $+6\cdot8$, and for women $D_L=15\cdot5\times$ body surface area $-0\cdot117\times$ age $+0\cdot5$; for both sexes the ratio of D_L to volume (VL) was $6\cdot49-0\cdot2098\times$ age $(\pm 1\cdot12)$, the correlation of $D_L:$ VL being highly significant.

In all cases in which lung volume was decreased there was some fall in D_L. Thus it was reduced in patients with pulmonary emphysema but not in those with asthma

or bronchitis without emphysema. However, there was a wide range for pulmonary diffusing capacity in normal subjects, so that the test offers poor differentiation of normal from abnormal. Patients with a high pulmonary blood flow showed increased diffusion and this became even more apparent when expressed per litre of lung volume. This last finding may have a limited usefulness in the diagnosis of left-to-right shunt in congenital-heart disease. The authors doubt the specificity of the alveolar capillary block syndrome and prefer to call it "inadequately functioning pulmonary parenchyma".

Excellent reproducibility was obtained in successive tests. There was good correlation between the pulmonary diffusing capacity and arterial saturation on exercise. A significant fall in oxygen saturation on exercise generally occurred with diffusing capacities of less than 8 ml. of CO per minute per mm. Hg. The authors conclude that the expense and inconvenience of the single-breath diffusing capacity test are not justified solely on the basis of its clinical usefulness.

G. M. Little

1165. Clubbing of the Digits: Physiologic Considerations F. A. BASHOUR. Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.] 58, 613-621, Oct., 1961. 27 refs.

At the University of Texas Southwestern Medical School, Dallas, 22 patients with moderate or marked clubbing of the digits have been studied. A comparatively small difference in arterio-venous oxygen saturation and tension was present in those with clubbing as compared with that in normal control subjects, there being no overlap between the two groups. Similarly a small difference in arterio-venous carbon dioxide content was observed in those with clubbing. There was no correlation between the duration or degree of the clubbing and the decrease in oxygen saturation, but the smallest arterio-venous differences appeared in those with the shortest history of clubbing. These findings are consistent with the theory that in patients with digital clubbing arterio-venous shunts are present.

The following tests were then performed. Exposure of the patients' hands to cold water resulted in an increase in the arterio-venous oxygen and carbon dioxide differences, although in 3 of them these changes were small. This finding suggests that the effect of cold causes constriction of the arterio-venous communications, but that in the presence of maximally functioning arterio-venous anastomoses a slight decrease in the size of the lumen of the vessels following exposure to cold fails to decrease the amount of blood passing through, or that in some patients with clubbing of long duration these structures are no longer responsive to cold stimulus. The breathing of pure oxygen for 30 minutes resulted in a large alveolar-arterial oxygen tension gradient, which indicated the presence of an intrapulmonary right-to-left shunt, averaging about 20% of the cardiac output. A subsidiary study of 8 patients with cirrhosis of the liver revealed that abnormalities were found only in the presence of associated clubbing or palmar erythema.

The author states that these observations are in agreement with Beclère's theory put forward in 1901 that in clubbing a "chemical substance", normally destroyed in the lungs, is passed through pulmonary shunts unaltered, producing peripheral dilatation. They also support the idea that reduced tissue oxygen tension, secondary to blood shunting, is the cause of the clubbing of the digits.

A. Gordon Beckett

1166. Correlation of Anatomic Pulmonary Emphysema and Right Ventricular Hypertrophy

J. B. CROMIE. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 657-662, Nov., 1961. 5 figs., 3 refs.

The author, working at Bellevue Hospital, New York. set out to resolve the discrepancy which so often appears to exist between the apparent anatomical severity of emphysema and the degree of right ventricular hypertrophy. To this end he has studied whole lung sections prepared, after appropriate lung injection, by the technique of Gough and Wentworth, with the application of a grid of 1-cm. squares. A standard of 8 grades ranging from "normal" to complete lack of alveolar tissue was adopted and by applying this to grid counts of a lung section the "average degree of emphysema for the whole lung" was computed. The degree of right ventricular hypertrophy and dilatation was determined at necropsy by noting the size of the ventricular cavity, prominence of the trabeculae, and thickness of the wall. "The size of the left ventricular cavity and its thickness, together with the state of the myocardium and the coronary arteries, was also noted". The whole heart, but not the dissected ventricles, was weighed.

Of 14 patients "with chronic bronchitis and emphysema" who had a "minimal degree of anatomic emphysema" 8 showed right ventricular hypertrophy and 6 did not, while of 16 "with chronic bronchitis and emphysema" having "moderately severe to severe anatomic emphysema" 7 showed right ventricular hypertrophy and 9 did not. It is stated that no causes of the ventricular hypertrophy (other than that of bronchitis and emphysema) were revealed at necropsy. When the two groups of patients with right ventricular hypertrophy were compared the greater average heart weight and greater thickness of the right ventricular wall were found in the group with the less severe emphysema. The author concludes that "there is no apparent correlation between the degree of anatomic emphysema of the lung and the degree of right ventricular hypertrophy and/or dilatation" and promises that "further correlation with clinical and physiologic studies are in progress".

[The problem here discussed is one of considerable importance and it is perhaps unfortunate that publication of this paper was not stayed until the promised clinical and physiological data were available to qualify it. For example, the author does not tell us the ages of his patients, whether or not any of them had validly established systemic hypertension, or indeed whether or not such hypertension was validly excluded, and if so, in which cases. It would have been helpful also to know details of blood volume and erythrocyte counts in these cases. Furthermore, the differential weighing of dissected ventricles, not carried out in this study, does seem

to provide additional information which is invaluable in the investigation of the problem.]

W. Raymond Parkes

INFLAMMATORY DISEASES

1167. Subclinical *Pneumocystis carinii* Pneumonitis in Adults

S. C. WOODWARD and W. H. SHELDON. Bulletin of the Johns Hopkins Hospital [Bull. Johns Hopk. Hosp.] 109, 148–159, Oct. [received Dec.], 1961. 3 figs., 17 refs.

Until 1956 it was thought that Pneumocystis carinii pneumonitis was virtually limited to early infancy. Since then 18 cases in adults have been reported, and this paper now describes a subclinical form of the infection in 2 adults, one of whom died of leukaemia and the other of lymphoma. Both patients had received prolonged treatment with corticosteroids, cytotoxic drugs, and irradiation. The lesions consisted of a slight focal interstitial pneumonitis with some infiltration of the septa by mononuclear and plasma cells, and with some large mononuclear cells and small numbers of Pneumocystis organisms in the alveoli. These changes did not produce noticeable clinical manifestations, nor did they alter appreciably the pre-existing long-standing disease, which seemed to represent an essential predisposing factor in the development of the infection.

Available evidence indicates that *Pneumocystis* is not a pathogenic agent in normal man, and that infection is primarily a reflection of deranged host resistance.

A. J. Karlish

Lung Abscess: an Analysis of the Massachusetts
 General Hospital Cases from 1943 through 1956
 H. I. Schweppe, J. H. Knowles, and L. Kane. New

England Journal of Medicine [New Engl. J. Med.] 265, 1039-1043, Nov. 23, 1961. 2 figs., 19 refs.

This paper describes the changing clinical picture of abscess of the lung as seen at the Massachusetts General Hospital, Boston. Between 1909 and 1942 there were 681 cases and between 1943 and 1956 a further 115 cases were seen, making a total of 796. The period is divided according to the type of treatment; up to 1933 this was mainly symptomatic, from 1933 to 1944 thoracic surgery was ascendant, while the period 1943–56 was the era of antibiotic therapy. The paper is particularly devoted to a review of the last 115 cases, in which the diagnosis was established by the finding of an air fluid level in the chest radiograph.

The incidence of the disease during the last part of the period fell from 10.8 per 10,000 admissions in 1944 to 2.2 per 10,000 in 1956, the total number of cases being 17 in 1944 and only 5 in 1956. The ages of the patients ranged from 3 months to 72 years, with a mean of 45 years; 86 patients were male and 29 female. Of the 115 cases the abscess was of less than 6 weeks' duration in 45 (39%) and of more than 6 weeks' duration in 45 (39%) and of more than 6 weeks' duration in 70 (61%). The commonest predisposing factors were disease of the teeth and gums, respiratory infection, alcoholism, tonsillectomy, and general anaesthesia. In 84 cases the abscess was single and in 31 it was multiple;

there were 108 abscesses on the right side, 36 in the posterior segment of the upper lobe and 20 in the apical segment of the lower lobe, while 40 abscesses were on the left side, 12 being situated in the apico-posterior segment of the lower lobe and 11 in the apical segment of the lower lobe α -Haemolytic Streptococcus was found in 74 cases, β -haemolytic Streptococcus in 26, Staphylococcus aureus in 14, and Escherichia coll in 9. In general the symptoms were much the same as those recorded in the past, but it was particularly noted that 37 patients had clubbing of the fingers. Among the 115 patients the over-all mortality was 8.7%, 10 deaths occurring during treatment

The last occasion on which rib resection and external drainage of an abscess was performed was in 1950. More recently surgical treatment has consisted in pulmonary resection. In 2 cases a right pneumonectomy was performed, in 2 lobectomy, and in 2 segmental resection. The most usual antibiotic treatment at the present time is either with penicillin alone or penicillin in combination with sulphadiazine or streptomycin. The mortality of 8.7% shows a striking reduction from that of 75% between 1909 and 1925. The decline in incidence is probably due to the advent of antibiotics, since if this form of treatment is initiated early in the course of the disease the great majority of cases can be cured by this means alone and before an abscess really develops.

Kenneth M. A. Perry

1169. Tracheotomy for Acute Respiratory Infections in Emphysema

L. H. HARRIS and J. HOUSTON. Lancet [Lancet] 2, 1170-1172, Nov. 25, 1961. 5 refs.

The authors describe 16 patients (15 male and one female, aged 38 to 68 years) admitted to Aintree Hospital, Liverpool, between the beginning of March, 1960, and the end of February, 1961, who were emphysematous and also had acute respiratory infections for which tracheotomy was performed. Of the 16 patients 9 had pneumonia, 6 had purulent bronchitis, and one had a lung abscess. Assisted ventilation was needed in 7 cases, 4 of which were fatal. One further patient died from pulmonary tuberculosis and heart failure. The patients were given the usual treatment, which included postural drainage and administration of antibiotics, bronchodilators, diuretics, digoxin, and oxygen. Some, who were seriously ill, were also given corticosteroids.

Aminophylline given intravenously seemed the most effective bronchodilator, while nikethamide intravenously in doses of up to 12 ml., or as an infusion of 12 ml. in 500 ml. of saline daily, sometimes made it unnecessary to give assisted ventilation. Carbon dioxide (CO₂) narcosis for which artificial ventilation was required occurred in 7 patients. The authors state that dichlorphenamide was not effective in lowering the pCO₂. Of the 5 patients who died 4 had received automatic intermittent positive-pressure respiration (I.P.P.R.) and this, it is thought, may have been partly responsible for the deaths, since the patients were receiving only 25 to 30% oxygen, whereas with manual ventilation 100% was given. In a later patient, who needed automatic I.P.P.R., 50 to 55% oxygen was used, with good effect. The authors point

out that once tracheotomy has been performed and secretions aspirated the pCO₂ is likely to fall, and humidified 100% oxygen can then safely be given at a rate of 2 litres a minute. A cuffed tube is used in order to reduce the dead space and permit I.P.P.R. and estimation of the pCO₂. There has been no difficulty in "weaning" patients from the tracheotomy tube, even when it has been retained for 37 days. The following are considered to be the advantages of tracheotomy: (1) secretions may readily be aspirated; (2) dead space is reduced and oxygen requirements therefore lowered; (3) excess CO₂ is "blown off"; and (4) I.P.P.R. is facilitated.

From their experience the authors conclude that tracheotomy should be carried out early rather than late, even if this means "performing a certain number of possibly unnecessary operations". Arthur Willcox

1170. Aerosolized Pancreatic Dornase and Antibiotics in Pulmonary Infections. Use in Patients with Postoperative and Nonoperative Infections

R. SPIER, E. WITEBSKY, and J. R. PAINE. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 878–886, Dec. 2, 1961. 4 figs., 13 refs.

The study here reported was undertaken at the Buffalo General Hospital, New York, to evaluate the use of aerosols of pancreatic dornase as an adjunctive treatment in acute and chronic pulmonary infections. The assumption underlying the study was that this enzyme is an effective lysing agent for thick, tenacious sputum. The 30 patients taking part, who suffered from conditions ranging from severe staphylococcal pneumonia and lung abscess to mild segmental pneumonia, were all treated with recognized systemic antibiotics in addition to the aerosols, which contained dornase mixed with various antibiotics. The authors consider that the addition of the aerosols was a therapeutic success.

[In view of the fact that at least 3 different preparations were used in treating these patients, it is quite impossible to assess the relative value, if any, of the aerosol of the pancreatic enzyme dornase.]

John Fry

NEOPLASTIC DISEASES

1171. Lung Cancer in Venice: an Epidemiological Study E. L. WYNDER, E. FERRARI, and E. FORTI. Lancet [Lancet] 2, 1347-1349, Dec. 16, 1961. 3 figs., 13 refs.

There is little air pollution from motor vehicles or industry in Venice, so that this factor cannot be an important cause of lung cancer among its inhabitants. It is, therefore, notable that in the hospital which serves Venice (and no other area) lung cancer is the commonest type of cancer to be diagnosed at necropsy as the cause of death in men—constituting 28% of all deaths from cancer; among women it accounted for 5% of such deaths. Other studies have shown that the mortality from lung cancer is at least as high in Venice as in other Italian cities.

Information about smoking habits, residence, and occupation was obtained for 63 men and 6 women with

lung cancer. For the 53 men and 5 women in whom the diagnosis was confirmed at necropsy and who had died between 1958 and 1960 the information was obtained from close relatives or friends, and for the remaining patients by personal interview. Control data were obtained from 200 male and 100 female patients in the same hospital and of the same ages as the patients with lung cancer but not suffering from a respiratory disease. The results showed that: (1) practically all the patients had lived in Venice for at least 20 years; (2) there were somewhat more labourers among the patients with lung cancer than among the controls, but there was no clear excess of men employed in any specific occupation; and (3) the patients with lung cancer included significantly fewer non-smokers and significantly more heavy cigarettesmokers. Richard Doll

1172. The Incidence of Lung Cancer in Finland and Norway

A. KORPELA and K. MAGNUS. British Journal of Cancer [Brit. J. Cancer] 15, 393-408, Sept., 1961. 10 figs., 4 refs.

There are many similarities between Finland and Norway—both are Northern countries with a low density of population, neither is heavily industrialized, and the total populations are about equal, as are also the populations of their two capitals. Of the two, Finland is the more agricultural, yet the vital statistics for lung cancer show a much higher mortality than in Norway. One difference between the countries is the age distribution of the population, Finland having one of the youngest populations in Europe, whereas Norway has one of the oldest. It is therefore essential to use age-standardized rates for all comparisons.

Mortality data, available for both countries from 1936, show that in each the crude male mortality from lung cancer increased sixfold between 1936 and 1958, but the mortality in Finland was about 6 times that in Norway throughout this period. The increase in female mortality from lung cancer was less marked; the Finnish mortality, however, increased more rapidly and by 1958 was almost double the Norwegian figure. In both countries the urban mortality has been greater than the rural; but in Finland the rural mortality has increased pari passu with the urban, whereas in Norway the increase in the rural rates has been less marked. Morbidity data are available for both countries for the period 1954-7, based on notifications to the two national cancer registries. Agespecific rates show that the female morbidity rate increased in both countries up to the oldest age groups; in males, however, the maximum morbidity rate in Finland occurs in the age group 65-69 years, whereas in Norway it occurs at 60-64 years. Age-standardized morbidity rates show that the incidence of the disease is 5.5 times higher in Finland among men and 1.9 times higher among women than in Norway. In both countries the urban morbidity is greater than the rural; but for both sexes, the ratio between the urban and rural rate is greater for Norway than for Finland. The results obtained for mortality and morbidity data are in close agreement. Richard Doll

Urogenital System

1173. Treatment of Urinary-tract Infections with Ampfellin: a Clinical Trial

W. Brumfitt, A. Percival, and M. J. Carter. *Lancet* [Lancet] 1, 130-133, Jan. 20, 1962. 9 refs,

The authors report a trial of ampicillin ("penbritin"). a new penicillin which has been reported to be more active against a number of Gram-negative bacteria than other penicillins. Taking part in the trial were hospital in-patients and patients seen in domiciliary practice, all with acute urinary-tract infections of less than one week's duration and a bacterial count above 100,000 per ml. of urine. These were divided into 2 roughly comparable groups; 45 patients were treated orally with 500 mg. of ampicillin every 8 hours for 5 days, and 34 patients with 100 mg, of nitrofurantoin orally every 6 hours for 5 days. The cure rates 2 days after the end of treatment were 93% for the ampicillin-treated group and 65% for the nitrofurantoin-treated group. Some weeks later, however, the cure rates had fallen to 84% and 56% respectively. Cure rates were high in patients with Escherichia coli infections, being 23 out of 28 (82%) for those treated with ampicillin and 15 out of 20 (75%) for those given nitrofurantoin. In Proteus mirabilis infections, however, the cure rates were 8 out of 11 for ampicillin and none out of 6 for nitrofurantoin. In the ampicillin-treated group one patient had a sensitivity reaction consisting of fever, erythema multiforme, and laryngeal stridor, and another patient developed Monilia vaginitis.

Bacterial sensitivities of the organisms isolated from infected urine were determined by the antibiotic-impregnated paper disk technique. Of the 241 organisms, 67% were found to be sensitive to disks containing 25 µg. of ampicillin. The majority of strains of E. coli, Streptococcus faecalis, and Pr. mirabilis were sensitive, but other Proteus organisms, Pseudomonas pyocyanea, and Aerobacter aerogenes were usually resistant.

K. G. Lowe

1174. Steroid Therapy of the Nephrotic Syndrome in Children: a Ten-year Material

H. C. SOMMERSCHILD. Journal of the Oslo City Hospitals [J. Oslo Cy Hosp.] 11, 188-200, Nov., 1961. 19 refs.

The results of steroid therapy in 15 children (6 male and 9 female, aged 5 months to 6 years) with the nephrotic syndrome are reported in this paper from Ulleval Hospital, Oslo. The patients were observed during the period 1950 to 1959 and the diagnosis was based on the presence of oedema, proteinuria, hypoproteinaemia, and hypercholesterolaemia and on the absence of hypertension and azotaemia. All were admitted to hospital within a few weeks of the onset of symptoms.

One patient had a spontaneous remission in hospital and was not given steroids. Of the remainder, 6 received corticotrophin (ACTH), in a dosage of 25 to 100 mg. daily, 4 were given prednisone (5 to 40 mg. daily), 3

received ACTH and prednisone, and one cortisone (40 to 100 mg. daily) and ACTH. Initial short-term treatment was for 10 to 20 days and maintenance therapy was continued for a further period varying from 4 to 36 months. One patient died and one has persistent proteinuria. Although 7 of the remaining 13 patients had at least one relapse after treatment, all 13 eventually became free of symptoms for periods varying from 18 to 104 months—up to the end of the study period.

Hewett A. Ellis

1175. Study of Some Aspects of Thyroid Function in Lipoid Nephrosis. (Étude des aspects du fonctionnement thyroidien au cours de la néphrose lipoidique)

N. Neimann, M. Pierson, G. Gentin, J. Martin, F. Georges, and C. Burg. Archives françaises de pédiatrie [Arch. franç. Pédiat.] 18, 420-458, April [received Nov.], 1961. 4 figs., bibliography.

The question of thyroid function in patients with nephrosis remains controversial. The idea that thyroid insufficiency was linked with nephrosis was abandoned when it was shown that the protein-bound iodine level was often increased in these patients and that there were signs of hyperthyroidism in lipoid nephrosis. At the Clinique Médicale Infantile, Nancy, the authors have investigated 17 patients (13 boys and 4 girls) with lipoid nephrosis. In 8 of these patients the disease appeared to be primary, in 4 it occurred after tonsillitis, in 2 following haematuria, and in 3 after T.A.B. vaccination; it was a true nephrosis in 12 cases and associated with nephritis in 5. All the patients were normally developed children, both physically and mentally, and showed no clinical signs of hypothyroidism.

A goitre was present in 6 patients. In one 12-year-old boy it appeared within 4 weeks of the occurrence of generalized oedema, but in another case after a delay of 6 years; the goitre disappeared when thyroxine was given. The estimated weight of the thyroid gland was considerably increased in 9 out of 12 cases in which it was investigated. The uptake of radioactive iodine was shown to be increased in 14 of the 16 cases so studied. The 2 with normal uptake values were among those patients without a goitre. Two prepuberal girls, aged 14 and 12 years, showed a high avidity for iodine which could not be related to the nephrosis with certainty. The protein-bound iodine level was constantly low, but its significance is not fully understood; a theory is put forward which, it is admitted, would need further confirmation. The total excretion of iodine in the urine was not increased. The proportionate distribution between triiodothyronine and thyroxine was higher in the urine than in the serum. The thyroid hypertrophy in so many of these patients was the more remarkable, as there was no evidence of lack of iodine in the diet.

[The findings are very interesting, but the deductions made from them need further discussion.]

V. C. Medvel

Endocrinology

THYROID GLAND

1176. Cerebellar Myxoedema. (Le myxœdème cérébelleux)

A. GUICHARD and P. PALIARD. Revue lyonnaise de médecine [Rev. lyon. Méd.] 10, 1117-1132, Nov. 30, 1961 [received Jan., 1962]. 30 refs.

Symptoms and signs of cerebellar disorder have only infrequently been described in association with myxoedema. The authors have found, and here summarize, 13 such cases reported in the literature between 1910 and 1936, as well as the 6 cases described by Jellinek and Kelly in 1960 (*Lancet*, 2, 225). To these 19 cases they add descriptions of 4 patients seen personally in the course of about 20 years (the first in 1942), and discuss the syndrome, which may occur in either of two forms in which the myxoedematous symptoms and the cerebellar symptoms predominate respectively. The disorder usually occurs in elderly women, and responds to treatment with thyroid hormone. *G. C. R. Morris*

1177. Carpal-tunnel Syndrome Associated with Myx-edema

D. C. PURNELL, D. D. DALY, and P. R. LIPSCOMB. Archives of Internal Medicine [Arch. intern. Med.] 108, 751-756, Nov., 1961. 8.refs.

At the Mayo Clinic, Rochester, Minnesota, the authors studied 10 patients in whom untreated myxoedema was associated with the carpal-tunnel syndrome in both wrists. Of the 9 patients studied by electromyography, 7 showed prolonged latency of response of the thenar muscles to stimulation of the median nerve just proximal to the carpal tunnel. This latency returned to normal in 2 patients who were treated with thyroid extract. Four patients had complete relief of subjective discomfort when treated with thyroid extract, and in 4 others the subjective manifestations were much improved. None of the patients receiving thyroid treatment required surgical decompression.

The authors consider that the compression of the median nerve in the carpal tunnel is due to the presence of myxoedematous tissue.

Charles Rolland

1178. Clinical Evaluation of the Thyroid Stimulating Hormone Activity in Exophthalmos. [In English]

S. B. BJÖRKMAN, T. DENNEBERG, and I. HEDENSKOG. Acta endocrinologica [Acta endocr. (Kbh.)] 38, 577–584, Dec., 1961. 2 figs., 12 refs.

Evidence concerning the relationship between exophthalmos and the secretion of thyroid stimulating hormone (T.S.H.) by the pituitary gland is conflicting, partly on account of the technical difficulties encountered in the assay of thyrotrophin. In this paper from the University of Lund, Sweden, the authors describe a new method for detecting the presence of a thyroid stimulating factor in

the blood of exophthalmic patients, which consists in transfusion of the patient's blood to a euthyroid subject. After withdrawal into a citrate-dextrose solution, 265 ml. of blood is transfused into the recipient, whose thyroid function during the next 72 hours is then studied by repeated estimations of the serum protein-bound iodine (P.B.I.) level.

In various trials carried out to test the method it was shown that the transfusion of blood from each of 2 healthy control subjects produced an insignificant increase in the serum P.B.I. level in the recipients. Similar negative responses were noted after the transfusion of blood from 2 exophthalmic patients, of whom one had only slight exophthalmos of recent development and the other had exophthalmos of 8 years' duration which had been stationary for 3 years. The remaining 6 patients, who were not hyperthyroid at the time, had exophthalmos which had recently been progressing. Transfusion of blood from these 6 produced a rise in the serum P.B.I. level in the recipients of between 20 and 50%, the maximum response usually occurring about 48 hours after the transfusion. One recipient received first a transfusion from a normal control subject with negative result, and then from an exophthalmic patient, which produced a positive result. This recipient was then on two occasions given an injection of a commercial preparation of T.S.H.; on each of these occasions the response was similar to that following the transfusion from the exophthalmic patients, suggesting that the thyroid stimulating action detected in the transfused blood was due tothyrotrophin. H.-J. B. Galbraith

1179. Familial Incidence of Diabetes in Hyperthyroidism L. V. Perlman. Annals of Internal Medicine [Ann. intern. Med.] 55, 796-799, Nov., 1961. 14 refs.

The relationship between diabetes and hyperthyroidism was studied in 187 hyperthyroid patients at the Grace-New Haven Community Hospital, New Haven, Connecticut. The incidence and family history of diabetes in this group of patients were compared with those in a control group of 187 patients of similar age and sex distribution. There were 13 diabetic patients in each of the 2 groups, the other diagnoses in the control group including gastro-intestinal, gynaecological, cardiovascular, infective, neoplastic, and functional disorders.

There was a significantly higher incidence of diabetes in the family history of the hyperthyroid patients. In addition, the hyperthyroid patients with a diabetic family history had significantly higher blood iodine levels and, to a less extent, radioactive iodine uptakes than those with no family history of diabetes, suggesting that the former were more thyrotoxic than the latter. The age of onset of hyperthyroidism did not differ significantly between those with and those without a diabetic family history.

The literature concerning the relationship between diabetes and hyperthyroidism is briefly reviewed, and the author concludes that diabetes predisposes patients to hyperthyroidism by some unknown mechanism.

Gerald Sandler

1180. Neurologic and Muscular Manifestations of Hyperthyroldism. [Review Article]

J. LOGOTHETIS. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 533-544, Nov., 1961. Bibliography.

1181. Hyperthyroldism in Subjects over 60 Years of Age (with Reference to 86 Cases). (L'hyperthyroldie du sujet agé de plus de 60 ans (à propos de 86 cas))

L. DE GENNES, M. L. BATRINOS, L. MOREAU, and H. DESCHAMPS. Presse médicale [Presse méd.] 69, 2425—2427, Dec. 9, 1961. 40 refs.

The authors assert that only recently have clinicians begun to appreciate the incidence of thyrotoxicosis in patients over the age of 60. Over the past 4 years, of all patients with hyperthyroidism seen at the Hôpital Broussais, Paris, 86 (20%) were in this older age group, pointing to the necessity of constant awareness of the possibility of "masked" hyperthyroidism in such patients. In all 86 cases the disorder was characterized by its insidious onset and atypical form, the classic presentation of symptoms and signs being seldom seen, so that in most instances there was a lapse of 2 years before the diagnosis was made. In 33 (38%) of the patients the onset was found to follow an emotional shock, 8 developed the disease after a febrile illness, while in the remainder no clear precipitating factor could be traced. Asthenia was the most constant finding, with a weight loss varying from 4 to 30 kg. One-third of the patients complained of anorexia and two-thirds of palpitations, although most of them (84%) had persistent tachycardia. Varying degrees of cardiac failure were noted in 31.4%, psychic upsets in 58%, heat intolerance in 58%, excessive thirst in 38%, diarrhoea in 16%, and tremor in 58%. The thyroid gland was palpably enlarged in only 52%, and in half of these cases it was nodular. Exophthalmos, although recorded in 64%, usually consisted only of some retraction of the upper eyelid.

Laboratory investigations of iodine metabolism were made difficult by the frequency with which these patients had been given iodides for other reasons, such as cough, but in the 82 patients in whom the uptake of radioactive iodine was determined the reading at 6 hours (found to be the most satisfactory differentiating time) was over 60%—that is, within the hyperthyroid range—while the protein-bound iodine level ranged from 9 to 18 μ g., with a mean of 10 μ g., per 100 ml. The basal metabolic rate was 50% above normal in 41 6% of the cases. Ancillary tests, which revealed a raised serum cholesterol level and increased reflexia, were occasionally of diagnostic value.

Administration of ¹³¹I was found to be the most satisfactory form of treatment. Of the 73 patients so treated 54 required only one dose, 17 two doses, and 2 three doses. Relief of signs and symptoms began 10 to 20 days after the start of therapy and was complete in 3

months. In the 22 patients with cardiac disease satisfactory improvement was obtained, 18 of them showing compensation and reduction in fibrillation. This latter group were usually kept in hospital to avoid the complicating exacerbation occasionally seen 2 to 3 weeks after therapy. Surgical treatment was limited to those patients whose thyroid glands were blocked by previous stable iodine therapy.

Allene Scott

1182. Incidence of Hypothyroldism in the Elderly W. H. LLOYD and I. J. L. GOLDBERG. British Medical Journal [Brit. med. J.] 2, 1256-1259, Nov. 11, 1961. 4 figs., 8 refs.

Of 3,417 new patients referred to the Geriatric Unit of Oldham and District General Hospital in 2½ years, 17 were hyperthyroid and 58 considered to be hypothyroid. The average age of the latter was just over 70 years, and there were 9 males to 49 females. All were treated with L-thyroxine, commencing with 0.1 mg. daily and increasing as needed to a maximum of 0.3 mg. daily.

Seven patients died before their response to therapy could be estimated. Of the remaining 51, all lost weight, had relief of symptoms, and showed improvement in facies under treatment with L-thyroxine. The basal metabolic rate was recorded before treatment in 34 cases, in 23 (67%) of which the value was -15% or lower. Before treatment the uptake of radioactive iodine (1311) was less than 20% of the administered dose in 31 (66%) of the 47 cases so assessed. Serum protein-bound iodine was estimated in 8 cases, in 7 of which the level was less than 3 μ g. per 100 ml. A diagnostic index (Wayne, Brit. med. J., 1960, 1, 1) of signs and symptoms was used in all 51 cases and provided confirmatory evidence of diagnosis in 33 of them.

The high incidence of hypothyroidism in this group of elderly people is emphasized. It is suggested that the condition may commonly be confused with ageing. Treatment with L-thyroxine was beneficial, but the dangers of such therapy for those with cardiac insufficiency make it essential for close control to be kept.

E. H. Johnson

HYPERPARATHYROIDISM

1183. Studies of Calcium Metabolism in Hyperparathyroidism with Special Reference to the Calcium Tolerance Test. [In English]

H. Spencer-Laszlo, I. Lewin, and J. Samachson. *Acta medica Scandinavica [Acta med. scand.*] 170, 547–559, Nov., 1961. 1 fig., 27 refs.

Since "as yet no single test is diagnostic of hyperparathyroidism", the authors, at the Montefiore Hospital, New York, have attempted to evaluate the calcium tolerance test as an aid to diagnosis in this disease, and in this paper they report the results obtained with the test in 13 cases of proven hyperparathyroidism and compare them with those in 23 persons with normal calcium metabolism. In performing the test 500 ml. of 5% glucose in water to which has been added 50 ml. of calcium gluconate containing 469 mg. of calcium is infused over a period of 4 hours to patients in the fasting state. The

blood calcium concentration, and also the 24-hour urinary excretion of calcium and phosphorus, are determined on the day before, on the day of, and on the day after, the infusion. Tests were carried out preoperatively in all 13 cases, and in 11 of them at varying intervals after the removal of a parathyroid adenoma.

Preoperatively the blood calcium level was raised in 12 cases and the alkaline phosphatase value was normal in 11 cases; the urinary excretion of both calcium and phosphorus was increased. The characteristic (but not constant) findings in these cases immediately after the test but before operation were: hypercalciuria, approximately 75% retention of the infused calcium (the normal. average being 68%), a very small rise in the blood phosphorus level, and a fall in the urinary phosphorus excretion which was normal in 6 cases but less than normal in the remainder. The changes in the serum calcium levels at the end of the infusion were similar to those in the normal subjects. After operation the spontaneous calciuria decreased strikingly in all cases, though the calcium retention resulting from the test remained similar to that found before the operation in all but 2 patients, both of whom were found to have more than one parathyroid adenoma. In general the phosphaturia tended to decrease, but was still higher than the normal range and was as high as or higher than the preoperative value in 3 cases. The serum phosphate levels, however, which had risen only minimally at the end of the infusion, tended to increase to normal levels during the postoperative phase. G. S. Crockett

1184. Phosphate Abnormalities in Hyperparathyroidism W. R. Beisel, E. S. Gerard, K. G. Barry, E. G. Herndon Jr., W. H. Meroney, and L. H. Kyle. Metabolism: Clinical and Experimental [Metabolism] 10, 771–780, Oct., 1961. 2 figs., 24 refs.

At the Walter Reed Army Medical Center, Washington, D.C., several methods of evaluating the renal excretion of phosphate were compared in 18 patients with surgically proven hyperparathyroidism due to parathyroid tumour. All showed an increase in the renal clearance rate of phosphate except one who was in renal failure. The lower limit of renal tubular reabsorption of phosphate has not been clearly defined, but if this is taken to be 86% then all these patients had values below normal, but if 78% be taken as the lower limit then 8 were above this level. In 6 patients the phosphate excretion index was normal (an index above +0.12 is regarded by some authorities as being suggestive of hyperparathyroidism).

Determination of the phosphate clearance rate postoperatively showed that in 9 of the patients it fell to the levels associated with hypoparathyroidism; generally in those with clinical manifestations of hypocalcaemia the lowest postoperative clearance rates were obtained in those with the higher preoperative values. During the intravenous infusion of calcium none of the patients showed a fall in the clearance rate greater than 30% of control values, whereas normal subjects experienced a fall of more than 50%, that is, into the hypoparathyroid range. (This test was not conducted postoperatively in patients whose clearance rate was below 10 ml. per minute.) In 4 patients with rates above this level a return of normal responsiveness to the calcium infusion was shown. The need for these further investigations is revealed by the fact that 7 of these patients had a borderline increase in the serum calcium level and 5 showed normal urinary calcium excretion on a low-calcium diet initially. It is stressed that although some of these patients had long-standing disease, the biochemical disturbances were only slight. In all the serum phosphorus level was below normal, except for the patient with renal failure.

The authors conclude that the most informative single measure of abnormal renal phosphate excretion is determination of the renal phosphate clearance in response to calcium infusion.

A. Gordon Beckett

ADRENAL GLANDS

1185. Pathogenesis of Hypokalemic Alkalosis in Cushing's Syndrome

N. P. CHRISTY and J. H. LARAGH. New England Journal of Medicine [New Engl. J. Med.] 265, 1083-1088, Nov. 30, 1961. 2 figs., 32 refs.

Hypokalaemic alkalosis was found in 12 out of 43 patients with Cushing's syndrome investigated at the Presbyterian Hospital, New York. Of these 12, 5 had an adrenal neoplasm and the other 7 had adrenal hyperplasia associated in 3 cases with an extra-adrenal neoplasm. Determination of the secretory rate of aldosterone by the isotope-dilution technique in 6 patients, including 3 with hypokalaemic alkalosis, showed that this was normal in all 6. Plasma cortisol concentration was measured in all 43-patients, and the urinary steroid level in 7 of the hypokalaemic cases was compared with that in 13 of those without alkalosis. Cortisol secretion was significantly higher in the hypokalaemic group. Thus the plasma cortisol concentration (normally 5 to 20 μ g. per 100 ml.) showed a mean value of 30 μ g. per 100 ml. in the uncomplicated cases of Cushing's disease, but in those with hypokalaemic alkalosis it ranged from 22 to 125 (mean 55) μg. per 100 ml.

The authors suggest that the cause of the potassium depletion and metabolic alkalosis in some cases of Cushing's syndrome is a grossly excessive secretion of cortisol rather than oversecretion of aldosterone. They point out that hypokalaemic alkalosis was found not only in the patients with extra-adrenal carcinoma and draw attention to the high incidence of adrenocortical neoplasm in the hypokalaemic patients. E. H. Johnson

1186. Association of Cushing's Syndrome and Neoplastic Disease: Observations in 232 Cases of Cushing's Syndrome and Review of Literature

B. L. RIGGS JR: and R. G. SPRAGUE. Archives of Internal Medicine [Arch. intern. Med.] 108, 841-849, Dec., 1961. Bibliography.

This communication from the Mayo Clinic reviews the evidence for an association between Cushing's syndrome and neoplastic disease. In a survey of the literature the

authors have found reports of 58 cases in which neoplasm, other than pituitary and adrenocortical tumours, occurred in patients with Cushing's syndrome. Of these growths 18 were thymomata, 22 bronchogenic carcinomata, 8 pancreatic carcinomata, and 10 miscellaneous tumours. Soon after Cushing's syndrome was first described its occasional association with a thymoma was noted.

Between 1932 and 1958, 232 cases of Cushing's syndrome were seen at the Mayo Clinic, excluding those cases due to administration of exogenous corticosteroids or corticotrophin (ACTH). The adrenal glands were explored surgically or examined post mortem in 203 cases, when adrenal hyperplasia was found to be present in 151, benign cortical adenoma in 27, and cortical carcinoma in 25. In this series malignant tumours were noted in 13 (5-6%) of the cases and benign tumours in 9 (3-9%). Of the malignant tumours 3 were thymomata and 2 were tumours of the pancreas.

It is admitted that the series is too small to provide statistical support for a conclusion of causal relationship, but some features were noted that suggest this possibility and encourage further study. For instance, it is striking that a high proportion of the malignant tumours associated with Cushing's syndrome, both in the authors' series and in the cases reported in the literature, have been tumours of the thymus, lung, or pancreas. Onethird of these have been thymoma—a rare tumour. Further, it has been noted that some tumours in patients with Cushing's syndrome have occurred at an earlier age than would be expected. These and other findings suggest that in some instances the relationship between the syndrome and malignant neoplasm is more than coincidental. Kenneth Stone

1187. Adrenal Disorders. I: Cushing's Syndrome and Its Puzzles. [Leonard Parsons Memorial Lecture] L. WILKINS. Archives of Disease in Childhood [Arch. Dis. Childh.] 37, 1–8, Feb., 1962. 6 figs., 16 refs.

DIABETES MELLITUS

1188. Motor Nerve Conduction Velocity in Diabetes D. G. Lawrence and S. Locke. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 483–489, Nov., 1961. 4 figs., 16 refs.

A study was undertaken at the Joslin Clinic and New England Deaconess Hospital, Boston, Massachusetts, "to obtain information about changes in motor nerve conduction velocity in diabetes mellitus". Included were 114 diabetics with involvement of the peripheral nervous system and 73 diabetics without such involvement; 30 prediabetic subjects (with a strong family history but no clinical evidence of diabetes) and 23 healthy subjects were also studied. Motor nerve conduction velocity was measured in the ulnar, median, and peroneal nerves. The healthy and prediabetic subjects showed no difference in conduction velocity and were therefore combined for use as a control group. Fifty

diabetics with neuropathy and 50 without neuropathy, who were matched for age, were also compared with the controls.

While there was a significant reduction in motor nerve conduction velocity in each of the 3 nerves in the diabetics as compared with the controls, a much greater reduction was recorded in those with neuropathy than in those without.

The authors state that measurement of conduction velocity is a simple matter, but that interpretation of results is complicated, and they discuss means whereby alteration of conduction in the large, rapidly conducting nerve fibres can be estimated. They conclude that the decrease in motor nerve conduction velocity in diabetes mellitus indicates a subclinical affection of motor nerves fibres; the affection is independent of age, and nerves in the upper limb are affected equally with those in the lower limb. This effect may be present without clinical evidence of neuropathy.

E. H. Johnson

1189. Continuous Blood Glucose Measurements in Diabetics Given Phenformin Timed-disintegration Capsules C. Weller and M. Linder. *Metabolism: Clinical and Experimental [Metabolism]* 10, 669–677, Sept., 1961. 8 figs., 3 refs.

The authors have studied at Grasslands Hospital, Valhalla, New York, the effect of the oral hypoglycaemic diguanide phenformin in 8 selected ketoacidosis-resistant diabetic patients by the method of continuous blood sugar determinations carried out colorimetrically by means of the "autoanalyzer", which is briefly described. Before the start of the experiment oral hypoglycaemic agents and/or insulin were discontinued for 48/hours. The drug was given either in a dose of 50 mg, of ordinary phenformin or in a controlled-release dose of 50 or 100 mg. in "timed-disintegration" capsules. In 5 of the patients the observations were made in the fasting state and continued for periods up to 12 hours; in the 6th patient the experiment was carried out twice-once during the fasting state and on a second occasion while the patient took a regular diet during the period of observation. In the remaining 2 cases the patients took known amounts of food at regular mealtimes.

The results showed that in the fasting state a continuous fall in the blood glucose level was obtained, the effect usually becoming apparent about 15 minutes after ingestion of the diguanide. In one male diabetic aged 40 with the malabsorption syndrome the blood sugar level began to decline as usual after 15 minutes, but the rate of fall was slow and this was attributed to the poor absorption in this case.

While phenformin in timed-disintegration capsules exerted a hypoglycaemic effect for up to 12 hours, the effect of the unmodified form of the preparation lasted only about 4 hours. In discussing their findings, the authors point out that the pharmacodynamic effect of an oral hypoglycaemic agent may be affected by variations in the rate and completeness of absorption, variations in rates of metabolism and excretion, and the distribution of the drug in the various tissue spaces of the body, especially at its site of action, the net result of these

biophysical reactions being the lowering of the blood glucose concentration. By altering the rate and duration of absorption of a compound, its pharmacodynamic effect may be prolonged. To this end, some of the phenformin used in this study was made up in a capsule containing granules of varying size which had been coated so as to release the compound at varying intervals. This allowed the pharmacodynamic effects of the compound to be maintained for at least 12 hours. The authors acknowledge that the chemical effectiveness of any oral hypoglycaemic agent in the treatment of diabetic patients depends upon long-term administration. At the same time, they suggest that by increasing its duration of effect, as do the timed-disintegration capsules, its usefulness to patients is enhanced.

John Lister

1190. Use of Long-acting Phenformin (DBI-TD) with Insulin in Insulin-dependent Diabetes

M. FABRYKANT' and B. I. ASHE. Metabolism: Clinical and Experimental [Metabolism] 10, 684–688, Sept., 1961. 13 refs.

The authors report their observations on 50 diabetic patients who were treated at Bellevue Hospital, New York, with phenformin in combination with insulin for between 4 and 20 months. Of these patients 32 had previously been treated with insulin in combination with tolbutamide or chlorpropamide for periods of one to 4 years, but the other 18 had had to discontinue the sulphonylurea drug after a number of weeks because of side-effects or apparent ineffectiveness of action. The usual dose of phenformin was 100 mg. in a timed-disintegration capsule, providing a hypoglycaemic effect lasting for up to 12 hours; the treatment was given on an outpatient basis, and the previous dosage of insulin was unchanged.

The addition of phenformin capsules as a supplement to insulin proved "exceedingly valuable", an excellent response being obtained in 5 patients and a good response in 15 in the group of 21 "labile" cases, while of the 29 "stable" diabetics the results were excellent in 9, good in 17, and poor in 2. The subsequent reduction in insulin dosage, which became possible in all but 6 patients, ranged between 29 and 54% of the pre-treatment dose in labile patients, up to 20% in mild stable diabetes, and up to 45% in more severe cases. Apart from the 3 therapeutic failures all the patients obtained a smoother metabolic control than with insulin and tolbutamide and the long-acting phenformin capsules permitted a sustained control of the blood sugar level.

The authors point out that much work has been devoted to showing that the hypoglycaemic sulphonylureas act through the stimulation of the pancreatic islets, but little attention has been paid to the possibility that these drugs may influence carbohydrate economy without the intervention of insulin, a view which they themselves have postulated and one which, they believe, explains more readily the benefits derived from phenformin used as an adjunct to insulin. Apart from improving the stabilization of labile diabetic patients the combination of insulin and phenformin considerably improved the stable patients' sense of well-being, while the addition of

phenformin enabled a good response to be obtained in a proportion of patients previously unresponsive to insulin with tolbutamide.

John Lister

1191. The Hyperlipemic Effect of a Low-fat, High-carbohydrate Diet in Diabetic Subjects E. L. Bierman and J. T. Hamlin. Diabetes [Diabetes]

10. 432-437. Nov.-Dec., 1961. 5 figs., 39 refs.

The authors report that the feeding of a diet which contained no fat and in which 85% of the calories were supplied by carbohydrates to 6 diabetic patients at the Hospital of the Rockefeller Institute, New York, led within one to 4 weeks to a 2- to 4-fold increase in the plasma triglyceride concentration, as compared with that on an isocaloric basal diet in which 40% of the calories were derived from corn oil and 45% from carbohydrate. The serum phospholipid levels were slightly raised and evidence is given to show that the additional triglyceride is probably present as low-density lipoprotein. The effect is thought to be transitory and the patients' insulin requirements were not affected by the high carbohydrate intake. A similar hyperlipaemia has been described by authors in normal, hyperlipaemic, and hypercholesterolaemic subjects. F. W. Chattaway

1192. Blood Sugar Findings during Pregnancy in Normals and Possible Prediabetics

A. Hagen. Diabetes [Diabetes] 10, 438-444, Nov.-Dec., 1961. 5 figs., 15 refs.

A study of the fasting blood sugar levels, frequency and degree of glycosuria if present, and the results of oral and intravenous glucose tolerance tests carried out at the University Hospital, Copenhagen, on 28 healthy pregnant women and a comparison with the results of similar studies on the same subjects after delivery showed that there was a shift of carbohydrate metabolism towards the diabetic state during pregnancy. Similar results were obtained in a group of 41 women who had all previously given birth to at least one child weighing more than 4,000 g., but the incidence of abnormal glucose tolerance curves was higher in this group, this finding, together with an increased incidence of glycosuria, being most marked at the 7th month of gestation. A more detailed study of the results in the latter group revealed a subgroup of patients who showed marked obesity, a history of high fertility, and the delivery of large infants with a high perinatal mortality. The women in this subgroup had oral tolerance curves of the "lag" type, and are considered to be potential diabetics. F. W. Chattaway

1193. Diabetes Mellitus and Pregnancy: Further Experience with Control of Perinatal Fetal Mortality

A. L. COURT, P. H. FUTCHER, and W. N. LONG. Diabetes [Diabetes] 10, 445-451, Nov.-Dec., 1961. 15 refs.

In this paper the authors discuss the management of diabetic mothers during pregnancy and report the outcome of 97 "viable pregnancies" in 85 diabetic women delivered at Johns Hopkins University Hospital, Baltimore, between January, 1953, and December, 1958, the incidence of diabetic deliveries during this period being

0.5% (of a total of 18,972 deliveries). The incidence of toxaemia in these 97 pregnancies was 40.2% (39 cases); long-standing hypertension was shown to be more serious than pre-eclampsia. Important factors in the management of these patients were strict regulation of the diabetes, delivery at the 37th week if possible and by caesarean section if essential, and treatment of the infant as if it were premature. There were 18 perinatal deaths (including 12 stillbirths), of which 10 were considered to be preyentable, 7 of these occurring in mothers with uncontrolled diabetes.

F. W. Chattaway

1194. Results of Treatment of 160 Diabetics with Chlorpropamide. (Résultats du traitement de 160 diabétiques par le chlorpropamide)

P. KISSEL, G. DEBRY, A. GUIBERT, and J. P. VITTE. Presse medicale [Presse med.] 69, 2365-2367, Dec. 2, 1961.

This paper from the Diabetic Out-patient Clinic, Nancy, describes the treatment of 160 diabetics with chlorpropamide. Out of 149 diabetic patients who completed the trial good results were obtained much more frequently in those who were underweight. Patients receiving more than 40 units of insulin daily did not respond at all well to chlorpropamide, good results being obtained in only 10% of these cases. Of those requiring less than 40 units of insulin daily, however, good results in regard to diabetic control were obtained in 31%.

Among the side-effects observed were gastro-intestinal-upset and hypoglycaemic symptoms, the latter being severe enough in 2 cases to necessitate withdrawal of the treatment. In addition, post-prandial vasomotor symptoms were in some cases such as to require termination of treatment. The authors point out that in spite of the pronounced and lasting effect of chlorpropamide, treatment with this drug does require careful supervision and may easily give rise to a false sense of security in both physician and patient. Also careful follow-up is necessary during this form of treatment.

I. McLean Baird

1195. Tubular Reabsorption of Glucose in Diabetes Mellitus and Renal Glycosuria. (Über die tubulare Glukoserückresorption bei Diabetes mellitus und Diabetes renalis)

G. LISEWSKI and G. MOHNIKE. Zeitschrift für die gesamte innere Medizin und ihre Grenzgebiete [Z. ges. inn. Med.] 16, 913-919, Nov. 1, 1961. Bibliography.

From the Institute for Research in Diabetes, Karlsburg, and the Charité Hospital, Berlin, the authors report an investigation of the tubular reabsorption of glucose in 7 patients with diabetes mellitus and 3 with renal glycosuria. Of the former group of patients 3 were males and 4 females and they ranged in age from 22 to 60 years; in all but 2 of them the disease had been present for at least 10 years. All 3 patients with renal diabetes were women, 2 of them being sisters, and their ages ranged from 17 to 4β years.

Initial investigations, which included retinoscopy and measurement of the blood pressure, showed that 5 of the

patients with diabetes mellitus were hypertensive and showed signs of marked retinopathy. A 6th patient, who was pregnant, had early retinal changes. In 3 of the diabetic patients the plasma non-protein nitrogen level was raised to between 47.6 and 72.8 mg. per 100 ml. and these 3 patients also had a raised renal threshold for glucose. The 3 patients with renal glycosuria showed, as expected, a lowered renal threshold for glucose. The maximum tubular reabsorption of glucose was determined by serial estimations (at 15-minute intervals) of inulin clearance and plasma and urinary glucose levels, from which the filtration rates of glucose and its rate of excretion and reabsorption were calculated. During the progress of this investigation, which took up to 2 hours. the patients were given a continuous intravenous infusion of a 30% solution of glucose at the rate of 1.6 g. of glucose per minute, this having been preceded by the administration of some 23 g. of glucose to saturate the extracellular tissues.

On the basis of a normal value of glucose reabsorption of 375 ± 79.9 mg. per minute for males and 303 ± 55.3 mg. per minute for females, 4 of the patients with diabetes mellitus had markedly decreased reabsorption rates of between 58 and 170 mg. per minute; these 4 patients were those with retinopathy, of whom 3 had nephropathy and one pyelonephritis. In a further patient, a man aged 49 with renal and retinal changes, the maximum reabsorption rate was 395 mg. per minute, but in this case the diabetes had been present for only 2 years. All 3 patients with renal diabetes showed reduced reabsorption of glucose, the maximum rates being 177 mg. per minute in the 2 sisters and 249 mg, per minute in the 3rd patient. In 3 of the patients the reabsorption rate decreased still further during the course of the investigation, and this is interpreted as being due to exhaustion of the enzyme system in a kidney already damaged by the vascular changes of diabetes mellitus.

H. F. Reichenfeld

1196. Diabetes Mellitus and Cirrhosis of the Liver.

J. M. B. BLOODWORTH JR. Archives of Internal Medicine
[Arch. intern. Med.] 108, 695-701, Nov., 1961. 31 refs.

In this paper the records of 27,050 consecutive necropsies performed at Ohio State University, Columbus, Ohio, between 1937 and 1960 are analysed with reference to the association of cirrhosis of the liver and diabetes mellitus. Among this material there were 1,067 patients with cirrhosis of the liver (average age 54·1 years), 807 patients with diabetes mellitus (average age 52·9 years), and 62 patients with both these diseases (average age 60·5 years).

In the first 5,000 necropsies, performed between 1937 and 1944, 1.2% of the patients with cirrhosis also had diabetes mellitus, while 1.9% of the diabetics also had cirrhosis. In the last 5,000 necropsies (1955–60) 12.0% of the cirrhotics had diabetes and 10.5% of the diabetics had cirrhosis.

The author considers that there has been an increase in the incidence of cirrhosis of the liver in diabetics during the past 20 years, and that there is a statistically significant association between the two disorders.

Charles Rolland

The Rheumatic Diseases

1197. Rheumatic Fever, Chronic Non-specific Thyroiditis, and Hyperthyroidism. (Fiebre reumatica, tiroiditis cronica inespecifica e hipertiroidismo)

E. CESARMAN, P. SERRANO, F. QUIJANO, and E. G. MORENO. Archivos del Instituto cardiología de México [Arch. Inst. Cardiol. Méx.] 31, 430-446, July-Aug., 1961 [received Jan., 1962]. 6 figs., bibliography.

The authors present 6 case histories to illustrate the association between rheumatic heart disease and thyrotoxicosis as observed in 6 female patients between the ages of 20 and 40 treated at the Hospital of the National Institute of Cardiology, Mexico. The first patient, aged 34, had a history of rheumatic fever at the age of 5, followed by mitral stenosis with haemoptysis at age 30. Mitral valvotomy was performed, but she failed to improve and developed evidence of hyperthyroidism, which responded to antithyroid treatment. Histological examination of a thyroid biopsy specimen (illustrated) showed evidence of chronic (Hashimoto's) thyroiditis. The second patient, who was aged 29, had a past history of frequent tonsillitis, but no rheumatic fever. She presented with mitral stenosis, atrial fibrillation, and cardiac failure. Mitral commissurotomy resulted in improvement and a return to normal cardiac rhythm, but 6 months later she developed an illness manifested by arthralgia and a raised erythrocyte sedimentation rate, which was treated as rheumatic fever and slowly improved. In the following year she developed a large tender goitre, which responded to antithyroid treatment; a thyroid biopsy examination showed chronic thyroiditis. Very similar histories were recorded in the remaining 4 patients, who all had evidence of rheumatic fever and cardiac valvular lesions and later developed thyroiditis and/or thyrotoxicosis. In all 6 patients precipitating antibodies against polystyrene latex coated with thyroglobulin were demonstrated. These were not found in 16 control patients, including some with acute or chronic rheumatic heart disease, chorea, and tonsillitis or in 4 healthy control subjects.

[The over-all incidence of this association among women in this age group with rheumatic heart disease seen at the authors' hospital is unfortunately not stated, nor are any findings in regard to L.E. cells or the L.E. factor presented.]

Allan St. J. Dixon

1198. Antimalarial Therapy of Lupus Erythematosus R. K. Winkelmann, C. F. Merwin, and L. A. Brunsting. Annals of Internal Medicine [Ann. intern. Med.] 55, 772-776, Nov., 1961. 3 refs.

A long-term study of the therapeutic results achieved with antimalarial drugs in lupus erythematosus (L.E.) was carried out at the Mayo Clinic, the records being reviewed of 70 patients in whom the disease was diagnosed in 1952 and 1953. The patients were treated with quinacrine hydrochloride initially and with other anti-

malarials later. In 2 of the patients the original diagnosis was thought to be erroneous and one further patient could not be traced. Of the remaining 67 patients 9 died in under 5 years (3 from L.E., 4 from carcinoma or cardiovascular accident, and 2 from unknown causes), and 58 were followed up for 5 years or more.

The group of 67 patients included 5 with subacute systemic L.E., 7 with chronic generalized discoid L.E., and 55 with chronic localized discoid L.E. The maintenance dosage of quinacrine was 100 mg. daily. On the basis of the response the patients fell into 3 groups: (1) remission without relapse within 3 to 5 years (7) patients); (2) improvement but with relapses (50); and (3) no improvement (10). Patients who remitted showed improvement after 4 to 8 weeks, but in some remission occurred only after 4 years' treatment. One case history is reported, that of the only patient with subacute systemic L.E. who went into remission after 3 years of continuous therapy and has now lived 5 years without treatment or relapse. Of the 10 patients who failed to respond 8 had discoid and 2 had systemic L.E. Chloroquine was found to be less toxic than quinacrine. It is pointed out that the effect of these drugs is suppressive rather than curative, relapses being the rule rather than the exception. Some patients responded better to one drug than to another; in subacute systemic L.E. added antimalarials may make it possible to reduce the dosage of steroids. E. G. L. Bywaters

1199. Immunologic Manifestations of a Group of Patients with a Diagnosis of Discoid Lupus Erythematosus J. C. Bennett, L. S. Osment, and H. L. Holley. *Arthritis and Rheumatism [Arthr. and Rheum.]* 4, 490–499, Oct., 1961. 24 refs.

The authors, working at the Medical College of Alabama and the Veterans Administration Hospital, Birmingham, Alabama, studied 16 of the 32 patients who had been seen in the Dermatological Clinic with chronic discoid lupus erythematosus of at least 2 years' duration to detect clinical and laboratory evidence of systemic lupus erythematosus.

Ten of the patients were male and one patient had rheumatoid arthritis. The crythrocyte sedimentation rate was raised in 9 patients and the haemoglobin value low in one. Two patients had albuminuria. However, only one patient could be diagnosed as having probable systemic lupus crythematosus on clinical grounds.

Nevertheless, 9 of the patients had a raised serum globulin content, 2 gave a positive result in the L.E. cell test and 2 in Coombs's test, one had a positive Wassermann reaction (with negative Treponema pallidum immobilization reaction), and 3 gave skin reactions to homologous leucocytes. The latex fixation reaction was positive in 4 patients, and 10 patients gave a precipitation reaction with deoxyribose nucleic acid.

The authors conclude that many patients with the diagnosis of chronic discoid lupus erythematosus have some of the serological features of systemic lupus erythematosus and raise the question whether those patients in whom the tests give positive results are more likely to develop frank systemic lupus erythematosus than are others.

G. L. Asherson

CHRONIC RHEUMATISM

1200. Pleural Effusion and Rheumatoid Disease R. WARD. Lancet [Lancet] 2, 1336-1338, Dec. 16, 1961. 7 refs.

In this study the relation between rheumatoid arthritis and pleural effusion was investigated at the Royal Infirmary, Blackburn. During a period of 15 to 39 months the two conditions were found to be associated in 7 men aged between 25 and 66. In all of these the sheep erythrocyte agglutination test gave a positive result. The pleural effusion preceded the joint changes in 2 patients, but articular pain was the presenting symptom in 3 patients; in the remaining 2 cases the diagnosis rested almost entirely upon the laboratory findings. The investigations revealed no evidence of any other cause of pleural effusion such as tuberculosis or bronchial carcinoma.

The case records presented include an account of a man aged 50 who had a large right-sided pleural effusion, from which straw-coloured fluid was obtained on aspiration. The fluid contained no malignant cells or acidfast bacilli, and guinea-pig inoculation of the fluid yielded negative results. Biopsy showed infiltration of the pleura with macrophages. In the 8th week of the illness this patient developed severe pain and swelling in the knee-joints, wrists, finger-joints, and right elbow. At this stage the erythrocyte sedimentation rate (Westergren) was 60 mm, in the first hour. Cortisone therapy was employed and 3 months later the patient was discharged on a maintenance dose of methylprednisolone. Some 28 months after first admission radiological examination of this patient showed erosions in the head of the proximal interphalangeal joint of one finger and also general periarticular demineralization in both his hands.

Another patient, a man aged 57, gave a history of pain in the fingers. He was referred to hospital after an attack of pleurisy. X-ray examination showed a small right pleural effusion; 6 months later the fingers had developed spindle-shaped deformities.

A. Garland

1201. Diagnostic Significance of Hyperuricemia in Arthritis

A. I. Grayzel, L. Liddle, and J. E. Seegmiller. New England Journal of Medicine [New Engl. J. Med.] 265, 763-768, Oct. 19, 1961. 4 figs., 13 refs.

The diagnostic significance of raised serum urate levels in patients with gout or rheumatoid arthritis was studied at the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland. All the patients and a group of healthy controls received diets of a known purine

content. The mean serum urate level in the controls as determined by an enzymatic spectrophotometric method was 5·1 mg. per 100 ml. in males and 4·0 mg. per 100 ml. in females.

Small to moderate doses of salicylate caused a rise in the serum uric acid levels in 10 of the 13 male patients with gout and 3 of the 5 males with rheumatoid arthritis. The opposite effect was noted in 4 female patients with rheumatoid arthritis. A similar difference between the responses of males and females was observed in the group of healthy subjects. The only female in whom there was an increase in the serum urate level after salicylates was the daughter of a gouty patient. False high values for the serum uric acid level as determined by the colorimetric method were observed when the serum salicylate concentration exceeded 13 mg. per 100 ml., presumably due to chromogen derived from the salicylate; this effect was particularly noticeable in those gouty patients with renal disease.

From a further study of the difference between males and females in the response to salicylate the authors conclude that it may be related to a quantitative difference in the renal mechanism for the excretion of either uric acid or salicylate and that the lower serum urate levels found in females may be a reflection of the same process.

J. Warwick Buckler

1202. Studies with Radioactive Gold

J. S. LAWRENCE: Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 341–352, Dec., 1961. 6 figs.; 28 refs.

In view of the technical difficulties in the gold treatment of rheumatoid arthritis of estimating small quantities of the metal in body fluids, the author of this paper from Salford Royal Hospital and Walkden Clinic, Manchester, tried radioactive gold (198Au), which can be detected in the tissues by scanning methods in amounts far below those found during therapy. It was given to 10 patients suffering from rheumatoid arthritis, a scintillating counter being used to estimate zonal distribution throughout the body and a wet counter for determining concentration in blood, synovial fluid, and urine. A number of biopsy specimens (synovial membrane, skin, and articular cartilage) were subjected to gold assay. Approximately 1 ml. of a solution of sodium aurothiomalate containing 198Au was injected into the gluteal muscle. The solution was supplied in two batches each containing 50 mg. of aurothiomalate in 5 ml., the batches having a total activity of 5 mc. and 12 mc. respectively. In 2 of the patients 198Au was mixed with 25 mg. of natural gold.

The gold level in the plasma ranged from 0.11 to 0.17 mg. per 100 ml. on the first day after the injection; thereafter it fell gradually until at the end of the 2nd week it was 0.02 mg. per 100 ml., the level being directly proportional to the dosage given. The fall in the plasma level was slowest in 2 patients who had had large amounts of gold previously and had become resistant. The lowest plasma gold level was observed in 2 patients who were hypersensitive to gold, but there was no relationship between the plasma level and disease activity or between the latter and urinary excretion of gold. In one case

the gold concentration in a biopsy specimen was 0.67 mg. per 100 ml. when the plasma level was 0.01 mg. per 100 ml. The highest scanning counts were obtained over the site of injection and the right hypochondrium, while in the limbs counts were greatest proximally and diminished peripherally. Painful joints gave high counts more frequently than symptomless joints.

It is known that heavy metals act as enzyme inhibitors and it is suggested that gold compounds exert a local effect on inflamed tissue by this action on the enzyme concerned in the inflammatory process. D. Preiskel

1203. Interactions of Rheumatoid Factor with Immune Precipitate Containing Antibody of Human Origin M. HARBOE. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 363-368, Dec., 1961. 1 fig., 25 refs.

The behaviour of the rheumatoid factor with immune precipitates containing antibody of human origin was studied in vitro at the University Hospital (Rikshospitalet), Oslo. The immune preparation consisted of human 7S y-globulin antibody and "varidase" (which had been used in treatment) from the serum of a patient with peripheral arterial insufficiency. Different components of the rheumatoid factor, as defined by the Rose-Waaler test, F II latex fixation test, and agglutination reactions with erythrocytes coated with incomplete anti-D showed that all these components were adsorbed on to the specific precipitate containing human antibody. It remains to be shown whether the rheumatoid factor can react with human y globulin in vivo and whether such an autoimmune mechanism is of pathophysiological importance to the individual. G. W. Csonka

1204. Studies on the Isolation of Rheumatoid Factor K. James, D. Felix-Davies, and D. R. Stanworth. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 369-385, Dec., 1961. 2 figs., 25 refs.

This study was carried out at the Birmingham Medical School to evaluate the different methods used in the isolation of the rheumatoid factor in a high state of purity for antiserum production. The recovery of rheumatoid factor was measured after each procedure by the Rose-Waaler test and the fractions were assessed by total protein estimation, and by ultracentrifugal, immunochemical, and immuno-electrophoretic analyses. The methods tested included euglobulin precipitation followed by diethylaminoethyl cellulose chromatography, zone centrifugation, and Cohn low-temperature ethanol fractionation in various combinations. The sera of 10 patients with active rheumatoid arthritis and high Rose-Waaler titre were selected for the tests. Detailed analysis showed that the most efficient way of preparing rheumatoid factor in a high state of purity was by euglobulin precipitation by water dilution followed by zone centrifugation. Methods involving euglobulin preparation by prolonged dialysis against water or the addition of saturated ammonium sulphate, DEAE cellulose chromatography, and ultrafiltration techniques were found to lead to a considerable loss of serological activity. With the methods used it was impossible to separate the rheumatoid factor from 19S γ isoagglutinins. Increases in

serological activity have shown no evident change in $19S\gamma$ concentration as estimated immunologically.

G. W. Csonka

1205. The Age Distribution of the So-called Rheumatold Factor. (Zur Altersverteilung des sogenannten Rheumafaktors)

H. H. Sachse and H. Poser. Zeitschrift für Alternsforschung [Z. Alternsforsch.] 15, 191–200. Nov., 1961. 23 refs.

In this paper from the University of Greifswald the authors report the results of a serological investigation into the occurrence of the so-called rheumatoid factor among patients of various age groups suffering from rheumatic and non-rheumatic disorders. The latex fixation test of Singer and Plotz, with slight modifications, was used, good correlation having been obtained between the results of this test and those of the Waaler-Rose test. A total of 911 sera were examined, of which 38 came from patients with rheumatoid arthritis. Of these, 24 (63%) gave a positive latex fixation reaction compared with 39 (1.9%) positive results among the remaining 873 patients.

When the age distribution of positive reactors was analysed a significant rise was noted in the middle of the fourth decade and again at the beginning of the sixth decade, irrespective of the clinical diagnosis. The possible interpretations of these findings are discussed.

H. F. Reichenfeld

1206. A Lipid-protein Fraction in Rheumatoid Plasma Precipitable with Chondroltin Sulfate after Euglobulin Removal

G. P. Kerby, S. M. Taylor, and N. M. Langley. *Journal of Clinical Investigation* [J. clin. Invest.] 40, 1900–1905, Oct., 1961. 7 figs., 12 refs.

In this investigation carried out at Duke University School of Medicine, Durham, North Carolina, after removal by precipitation from human plasma of the euglobulin fraction by the mineral acid dilution method a further precipitate was obtained from the supernatant by the addition of chondroitin sulphate. The precipitate thus obtained is termed the S₁ fraction. It was strikingly. increased in quantity by dialysing the plasma against a standard buffer in the first instance. This was reversible by the re-addition to the dialysed plasma of an organic, heat-stable substance in the dialysate. Numerous known dialysable plasma components were examined without identifying the substance active in these procedures. The biological significance of the increased chondroitin sulphate precipitate seemed related to the group of acutephase reactants. A group of 26 patients with rheumatoid arthritis gave the highest lipid-protein fraction available for precipitation as S₁ fraction in comparison with 20 active inflammatory cases and 19 non-inflammatory cases. No quantitative differences were obtained by means of electrophoresis or Ouchterlony techniques, the latter showing the S₁ fraction to contain fibrinogen and lipoprotein among its components. The cholesterol element of the fraction was high, especially in rheumatoid plasma. The S₁-fraction inhibiting substance was also demonstrated in urine and cerebrospinal fluid.

Harry Coke

Neurology and Neurosurgery

1207. Carcinomatous Micrometastases of the Spinal Cord Imitating Progressive Muscular Atrophy. (Микрометаставы рака в спинной мовг, имитировавшие спинальную амиотрофию Дюшена—Арана)
М. N. KLINGMAN and V. D. KALINKA. Журнал Невропатологии и Психиатрии [Ž. Nevropat. Psihiat.] 61, 1630–1635, No. 11, 1961. 3 figs., 6 refs.

From the Medical Institute, Riga, the authors report a case which was initially thought to be one of progressive muscular atrophy but which was later shown to be due to micrometastases in the spinal cord. Attention is drawn to the selective and systematic character of the lesions in . the spinal cord and to the absence of visible metastases. The illness began with influenza and pneumonia and was followed within a month by general weakness, difficulty in getting up, and weakness of the arms and legs. On admission to hospital in the first month of illness the patient's arm reflexes were found to be absent and the leg reflexes weak. A diagnosis of spinal amyotrophy was made and when discharged during the 3rd month of the illness the patient had shown considerable recovery of muscular power and this was maintained until shortly before readmission during the 8th month. By this time there was now widespread atrophy of the muscles of the shoulder girdle, forearm, hands, thorax, thighs, and legs, and the patient could make very little movement of the limbs. Sensation, however, was intact, and although all the limb and abdominal reflexes were absent, there were no pathological reflexes. The patient died in the 10th month of the illness without any radiographic evidence of a pulmonary neoplasm having been found.

At necropsy, however, a tumour was found arising from the left upper lobe bronchus and affecting the bronchial and mediastinal lymph nodes; the tumour was of mixed round-cell and out-cell type. On section the spinal cord was found to be smooth and shiny and in places the distinction between grey and white matter was not clear. In the lower spinal segments there were small foci of softening and haemorrhage, but no metastases were visible to the naked eye. However, microscopical examination revealed metastases affecting the membranes and the lower cervical and upper thoracic regions of the cord, especially in the anterior horns and pyramidal tracts. Emphysema, bronchopneumonia, and coronary, aortic, and cerebral atherosclerosis as well as myocardial fibrosis and nephrosclerosis were also found. G. P. McGovern

1208. Nandrolone-phenpropionate in Progressive Muscular Dystrophy: a Preliminary Report

I. A. Brown and E. M. James. Archives of Pediatrics [Arch. Pediat.] 78, 421-431, Nov., 1961. 4 figs., 6 refs.

This preliminary study from St. Joseph's Hospital, St. Paul, Minnesota, describes the use of injections of nandrolone phenpropionate ("durabolin") over a

period of 8 months in 18 patients suffering from progressive muscular dystrophy. Clinical evaluation was difficult, but 6 patients showed subjective and only 2 objective improvement.\ In 14 cases there was a reduction in the urinary creatine excretion, and in 12 cases a reduction in the urinary creatinine excretion. The serum aldolase level was raised in 10 of the patients, and in 8 of these the level was reduced after 3 months' treatment. Muscle biopsy was performed before treatment was started, and in the majority of cases was repeated at the end of treatment, usually from the same muscle. It is stated that "in 80% of the cases" there was improvement in the histological appearance; this consisted in reduction of oedema in the muscle, greater uniformity of shape and size of the muscle fibres, and reappearanceof striations in the fibres. J. W. Aldren Turner

1209. Heparin Potassium in the Treatment of Chronic Multiple Scierosis

J. MASCHMEYER, R. SHEARER, E. LONSER, and D. K. SPINDLE. Bulletin of the Los Angeles Neurological Society [Bull. Los Angeles neurol. Soc.]. 26, 165-171, Dec., 1961. 2 refs.

The results obtained with heparin potassium in the treatment of chronic disseminated sclerosis are reported in this paper from Loma Linda University, Los Angeles. The drug was given by mouth to 10 patients with advanced disease, 2 tablets [size unspecified] being dissolved under the tongue 3 times a day after meals. All the patients were receiving a low-fat diet. Of the 10 patients 3 did not complete the 3 months' trial,

In 5 patients there was objective improvement, with lessening of intention tremor and increase in muscle power sufficient to allow chairbound patients to walk with a stick. While the authors freely acknowledge that such improvement might have occurred in spite of the treatment, they consider that these results justify further trial of heparin potassium in disseminated sclerosis.

- G. S. Crockett

1210. Heredofamilial Neuritis with Brachial Predilection J. C. Jacob, F. Andermann, and J. P. Robb. *Neurology (Neurology (Minneap.)*] 11, 1025–1033, Dec., 1961. 5 figs., 5 refs.

The authors, from McGill University, Montreal, describe 2 families in one of which 4 members and in the other 3 members had recurrent attacks of mononeuritis multiplex with brachial predilection. Severe pain usually preceded the development of muscle weakness, and the right arm was considerably more often involved than the left. The course was self-limiting, and good recovery of function usually took place. The "defect" appears to be transmitted by an autosomal dominant gene. The authors stress the similarity of the condition to neuralgic amyotrophy and serum neuritis. J. W. Aldren Turner

DIAGNOSTIĆ METHODS

1211. Theta-discharges in the Middle-line—EEG Symptom of Temporal Lobe Epilepsy

L. CIGÁNEK. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 669-673, Oct. [received Dec.], 1961. 3 figs., 15 refs.

This paper from the Institute of Experimental Medicine of the Slovak Academy of Sciences, Bratislava, reports a finding in the electroencephalogram (EEG) of patients with temporal-lobe epilepsy described as a theta discharge in the middle line. One or more EEGs were recorded from each of 50 patients aged 3 to 69 years with temporal epilepsy, the bipolar as well as the average reference technique being used. Theta discharges in the middle line were found in 18 (36%) of the cases in the group and had the following characteristics: localization in the anterior rather than in the middle or posterior parts of the midline; in 7 out of the 18 cases the discharges spread in a parasagittal direction to the side of the lesion, this being identifiable; only rarely did they spread to the temporal region or diffusely, tending to preserve their predominance and maximum amplitude in the anterior middle line. The frequency of these sinusoidal waves varied between 4 and 7 c.p.s. and with the average reference recording technique their amplitude was found to be 20 to 40 μ V.; they appeared less prominently in bipolar recordings. They were independent of, or synchronous with, the typical epileptic discharges which were sometimes recorded over the temporal lobes, and in some records they were, apart from slow dysrhythmia, the only EEG symptom of the clinical condition.

Three, cases are described in detail and extracts from the relevant records are shown, followed by a short discussion of the postulated anatomy and physiology underlying the discharges.

Peter Leyburn

1212. A Preliminary Note of the Effect of Hexafluorodiethyl Ether (Indoklon) on the Electroencephalogram of the Epileptic

A. A. Kurland, E. Delamonica, and C. Marshall. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 781–784, Oct. [received Dec.], 1961. 1 fig., 4 refs.

Previous studies carried out with hexafluorodiethyl ether ("indoklon"), used as a convulsant in psychiatric treatment, stimulated the authors of this paper from Spring Grove State Hospital and the Johns Hopkins Hospital, Baltimore, to carry out further observations on its effect on the EEG of the epileptic. Interesting features of the drug included the rapidity of its action (for example, the onset of a convulsion within 30 to 50 seconds of its administration) and the relatively wide range between the average convulsant dose and that needed to produce subclinical seizure patterns in the EEG.

The study was carried out on 26 ambulatory patients resident in an epileptic colony, most of whom were tested at least 3 times. Indoklon in a dose of 1 ml. of a 5% solution was injected into the median cubital vein

over 5 to 10 seconds after a resting baseline EBG record had been obtained. Transient discomfort was usually experienced at the time of the injection, most patients describing a burning pain radiating up the arm. Out of 52 records showing abnormalities during the resting, pre-indoklon phase, 24 showed changes following the injection, whereas of 19 normal resting pre-indoklon records, only 2 displayed a change. The types of abnormalitied induced by indoklon were: (a) paroxysms of generalized 3- to 4-c.p.s. spike-and-wave complexes; (b) multiple focal spikes; and (c) accentuation of the spontaneous abnormalities by an increase in voltage of generalized theta activity and an increase in the number of spike discharges.

It was noted that one group of patients with abnormal resting records consistently showed significant activations, whereas a second group with equally abnormal resting records were consistently refractory to attempted activation. No clinical differences could be found between the two groups and it seems possible that different mechanisms were being affected. The authors feel that this consistency of presence or absence of activation with repeated trials merits further study. They conclude from this pilot study that the main value of indoklon is that it appears to clarify underlying EEG pathology when present without creating new abnormalities.

Peter Leyburn

BRAIN AND MENINGES

1213. Subepicranial Hydroma: a Complication of Head Injuries in Infants and Children

J. A. Epstein, B. S. Epstein, and M. Small. *Journal of Pediatrics [J. Pediat.*] **59**, 562–566, Oct., 1961. 5 figs., 3 refs.

Subepicranial hydroma is a rare and benign complication of head injury in infancy. Linear fracture of the cranial vault, usually in the parietal area, allows cerebrospinal fluid to leak from the subarachnoid space into the potential space underlying the galea aponeurotica. The effusion is not restricted as in cephalhaematomata by suture lines and may spread over the whole surface of the vault, presenting a soft, non-crepitating, non-tender swelling. Transillumination will confirm the distinction from haematoma.

In this paper from the Long Island Jewish Hospital, New York, the authors report 13 cases, all associated with fractures of the vault. They emphasize the benign natural history of the condition and advise against aspiration of the hydroma because of the danger of introducing infection into the meninges.

J. B. Foster

1214. The Diagnosis of the Choroid Plexus Papilloma of the Lateral Ventricle

K. M. LAURENCE, R. D. HOARE, and K. TILL. Brain [Brain] 84, 628-641, Dec., 1961. 10 figs., 35 refs.

The authors, from the Hospital for Sick Children, Great Ormond Street, London, describe 5 cases of choroid-plexus papilloma of the lateral ventricle in children. In the first 3 cases a diagnosis of communicating hydrocephalus was made on the basis of clinical and

laboratory studies, including bubble ventriculography. After the ventriculography all 3 patients showed progressive deterioration and died within one to 3 weeks. In each case necropsy revealed a papilloma 4 to 6 cm. across in one lateral ventricle. Review of these cases showed the following common features: normal development for 7 months or more before the onset of hydrocephalus; the presence of papilloedema; cerebrospinal fluid under greatly increased tension and with raised protein concentration and cell count; symmetrical enlargement of the entire ventricular system with basal cisternal block as revealed by bubble ventriculography; and rapid clinical deterioration following ventriculography.

Subsequently 2 more cases presented with this clinical picture. The first of these, following rapid deterioration in the 3 days after ventriculography, was subjected to more extensive air studies, leading to the demonstration of an intraventricular mass. The patient died 5 weeks after operative removal of the tumour. In the second case, that of a boy aged $2\frac{1}{2}$ years, clinical deterioration followed ventriculography and a second, fuller, ventriculogram revealed a tumour the operative removal of which led to satisfactory recovery.

It is suggested that two factors contribute to the hydrocephalus in these cases: one is the basal cisternal block (seen in all 5 cases), which the authors attribute to recurrent small haemorrhages from the friable tumour; and the other is increased production of cerebrospinal fluid (which can be experimentally demonstrated) by the tumour. The authors conclude that in children presenting with hydrocephalus who show moderate papilloedema and severely increased cerebrospinal-fluid pressure with raised protein content and cell count, especially if there is an unfavourable reaction to ventriculography, choroid-plexus papilloma should be looked for by fuller air studies and, if found, removed promptly.

B. S. Meldrum

1215. Use of Radioactive Arsenic (As⁷⁴) in the Diagnosis of Supratentorial Brain Tumours.

E. H. BOTTERELL, W. M. LOUGHEED, T. P. MORLEY, R. TASKER, and W. PAUL. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 1321-1328, Dec. 16, 1961. 5 figs., 21 refs.

This paper records the results obtained at the Toronto General Hospital by using the brain-scanning apparatus developed at the Massachusetts-General Hospital by Brownell and Sweet (Nucleonics, 1953, 11, 41). It incorporates a pair of scintillators which can be placed at corresponding points on each side of the head for recording gamma radiation as a unilateral preponderance and also for recording a concentrated source of positron emission. These two procedures can be carried out at the same examination. The most convenient and useful source of positron emission was found to be radioactive arsenic (74As). The mechanical moving system consists of a horizontal bar holding the two scintillation detectors facing one another, the distance between the detectors being adjustable to clear the patient's head during their movement. The horizontal bar is carried through a uniform horizontal motion, undergoing a vertical descent at the completion of each horizontal excursion until the scanning has covered a rectangular area taking in the whole head. [The paper should be read for further technical details of the apparatus and the technique used.]

More than 350 patients were scanned, but this paper reviews only 203 later cases in which the technique was standardized. Of these 203 patients, 61 were rejected because the diagnosis was not verified. Of the remainder, 56 had no neoplastic disease and in 86 the presence of a supratentorial tumour was verified histologically. Of the 86 tumours, 45 (52%) showed a positive scan. Of 26 meningiomata 24 were demonstrated, as were 10 out of 37 gliomata. In general it was found that with decreasing histological malignancy of gliomata the likelihood of detection lessened. One of the gliomata was intensely vascular, but this was not detected.

The authors submit the following conclusions: (a) a positive scan always indicates an abnormality, and where tumour is suspected on clinical grounds alone the confirmation it provides may be judged sufficient to justify direct surgical approach without further special radiological investigation; (b) no inference as to the pathological nature of the lesion can be made from a positive scan; (c) a negative scan by no means excludes tumour from the diagnosis; (d) the role of the scan in the screening of a patient whose diagnosis hangs uncertainly between tumour and non-neoplastic disease is comparable to that of the electroencephalogram; (e) there is an important place for this method in the diagnosis of recurrent meningioma in that follow-up radioarsenic studies can, if the clinical picture demands it, be undertaken on an out-patient basis; (f) external scanning is regarded as a highly desirable diagnostic technique which in certain instances can supplant other methods. Variations in the technique involving instrumentation and choice of radioisotope will no doubt improve the present results. J. MacD. Holmes

1216. Cerebral Ischemia: Surgical Procedure in Cases Due to Tortuosity and Buckling of the Cervical Vessels J. H. HARRISON and P. A. DAVALOS. *Archives of Surgery [Arch. Surg.*] 84, 85–94, Jan., 1962. 12 figs., 7 refs.

Over a period of 3 years at Emory University School of Medicine, Atlanta, 240 patients with cerebral vascular disease were subjected to carotid and vertebral arteriography. Of these patients 46 were found to have "huckling" of the great years of the buckling" of the great vessels of the neck, the "buckles" being described as S-shaped deformities, complete loops, or V-shaped indentations of the vessels; they were usually bound to the surrounding tissues by dense fibrous bands. The internal carotid artery was involved in 40 cases, bilaterally in 16 of them. In 5 cases there was buckling of the vertebral artery, while buckles of the innominate artery were demonstrated in 2 and of the branches at their origin from the aortic arch in one. Corrective surgical treatment was carried out in 39 patients with 42 lesions, the operation consisting usually in excision of the buckled segment followed by end-to-end or end-to-side anastomosis. There was one death from thrombosis of the internal carotid artery in a patient with preoperative symptoms of transient ischaemic episodes. A frank hemiplegia had occurred shortly before operation in 11 patients, and in 8 of these the signs of hemiplegia cleared almost completely after the operation; 2 improved partially and one died. Of 12 patients who had symptoms of incipient stroke before operation, 2 were improved and one did not benefit. [The outcome in the remaining 9 is not stated.] Operation was performed on 14 patients with a history of transient attacks of cerebrovascular insufficiency; one of these died and the remaining 13 had no further attacks.

The authors consider that in patients with completed strokes and strokes in evolution there is little doubt about the significance of the lesions described in the production of cerebral vascular insufficiency, but that in the group with transient bouts of cerebral vascular insufficiency the present data are insufficient for an assessment of the effects of surgical correction of a buckled vessel.

[These results are interesting, but the data provided do not permit an evaluation of the relationship between buckling of vessels and the presence of signs of cerebrovascular insufficiency and of the beneficial effects of correction of the buckling.]

Bernard Isaacs

1217. Premonitory Symptoms of Cerebral Embolism C. E. Wells. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 490-496, Nov., 1961. 8 refs.

Of 120 patients with cerebral embolism seen at the New York Hospital-Cornell Medical Center, New York, in the period 1940-59, 19 gave a history of symptoms preceding the specific neurological dysfunction. Headache was the dominant symptom in 10 patients, occurring from a few minutes to 2 days before the stroke; in 5 of these patients the pain was localized to the side of the head which later became the site of the embolus, and in the other 5 the headache was generalized. Six patients had other types of premonitory symptoms. In 3 these consisted in a general feeling of being unwell preceding the stroke. The other 3 patients had focal warning symptoms, manifesting a transient neurological upset, which later was repeated with the embolism. The possible causes of these types of premonitory symptoms are discussed: whether they are caused by a single embolus moving along a vessel or by more than one embolus taking the same course. The author does not, however, consider there is yet enough evidence to support either of these possibilities with certainty.

In the remaining 3 cases in the series the premonitory symptoms were less obviously associated with the embolism.

E. H. Johnson

1218. Biperiden (Akineton) in Parkinsonism

W. H. TIMBERLAKE, R. S. SCHWAB, and A. C. ENGLAND JR. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 560-564, Nov., 1961. 12 refs.

Two clinical trials of biperiden ("akineton") in Parkinsonism are reported from the Massachusetts General Hospital and the Lemuel Shattuck Hospital for Chronic Diseases, Boston. In the first the effects of biperiden and procyclidine were compared in 23 hospital in-patients. After a period without treatment, a patient was given one or other of the drugs, and dosage was

increased until moderate side-effects (dry mouth or blurring of vision) were produced. Dosage was then reduced and the drug withdrawn, and the same procedure enacted with the other drug. A neurological test to estimate the anti-Parkinsonian effect of the drugs was performed every 2 days. Biperiden in doses of 8 to 24 mg. daily reduced tremor and rigidity in half the patients and improved the general performance in three-quarters. These results were somewhat better than with procyclidine. The incidence of side-effects with the two drugs was similar.

In the second trial biperiden was openly substituted for the previous medication received by 100 ambulatory patients. Dosage was increased to a level where side-effects began and then reduced; there was no definite time limit. Of the 100 patients, 53 preferred biperiden and elected to continue with it. The others found it less effective or that it caused worse side-effects, and returned to their previous medication.

The side-effects of biperiden are similar to those caused by belladonna and are immediately reversible on withdrawal of the drug. Biperiden can be taken in conjunction with antihistaminic agents and with drugs used to control tremor such as mepazine.

E. H. Johnson

EPILEPSY

1219. Intracarotid Amobarbital in Epileptic Patients: a New Diagnostic Tool in Clinical Electroencephalography R. L. ROVIT, P. GLOOR, and T. RASMUSSEN. Archives of Neurology [Arch. Neurol. (Chicago)] 5, 606-626, Dec., 1961. 12 figs., 31 refs.

The authors have studied at the Montreal Neurological Institute, Canada, the results of the intracarotid injection of amylobarbitone ("amytal") in 20 patients with intractable epilepsy, and in particular have examined the possibility of distinguishing by this method between cases of primary centrencephalic epilepsy and those due to a concealed primary cortical focus in which the electroencephalogram (EEG) showed secondary synchrony simulating that seen in the former group. In addition to such cases the series included some patients with restricted unilateral focal epileptogenic lesions in whom the EEG abnormalities were limited to the side of the lesion, and others with independent bilateral or multiple foci.

It was found that only in those patients with a single focal cortical lesion and limited EEG abnormalities, as also in those in whom a focal lesion was giving rise to secondary synchrony, were all epileptiform manifestations in the EEG suppressed by ipsilateral carotid injection of amytal. Centrencephalic epileptic discharges were not inhibited by injection of the drug into either of the carotid arteries, and indeed rhythmic slow-wave discharges were sometimes triggered off by the injection. The authors conclude that when complete inhibition of epileptic discharges in the EEG occurs following the injection of amylobarbitone, then the epileptic lesion must lie within the cortical area supplied by the artery concerned, and that this method can be used to distinguish

between cases of secondary synchrony resulting from a focal epileptic lesion and cases of primary centrencephalic epilepsy. The causes of physiological disturbances, in the form of augmentation of the paroxysmal centrencephalic discharges, brought about by the injection are discussed.

J. B. Stanton

1220. A Psychological Study of 29 Cases of Petit Mal. (Étude psychologique de 29 cas de petit mal)
M. L. ETCHEVERRY, P. VERGER, and P. LOISEAU. Annales de pédiatrie [Ann. Pédiat.] 38, 192–197, Jan. 14, 1962. 27 refs

The 29 cases of petit mal which formed the material for this study comprised 12 male and 17 female patients ranging in age from 5 to over 13 years. In 19 cases the attacks consisted of "pure absences", in 3 they were associated with automatism and in 3 with myoclonus, and 4 patients had akinetic attacks. The patients were given tests which included assessment of the intelligence quotient (I.Q.) on the Terman-Merrill scale, a visuomotor test, and the Rorschach test.

The I.Q. was above 110 in 5 cases, above 90 in 8, between 80 and 90 in 10, and below 80 in 6. Electroencephalography (EEG) showed that those patients with the higher I.Q:s had pure 3-per-second spike-and-wave EEG records free from interictal disturbances. Among disorders of character and behaviour the authors found slowness of cerebration in 16 cases, psychomotor instability in 6, and outbursts of impulsive behaviour in 11. These disturbances appeared in proportion to the number of attacks, and impulsive behaviour correlated closely with abnormalities in the EEG consisting of epileptic disturbances recorded predominantly from the anterior parts of the hemispheres or of background dysrhythmia. Organic stereotypes in the visuo-motor test were found to correlate particularly with clinical and EEG evidence of "absences", as did the appearance of epileptoid characteristics in the Rorschach test. J. B. Stanton

1221. Evolution of Petit Mal Epilepsy in Relation to Treatment. Clinical and Electroencephalographic Factors in Prognosis. (Évolution du petit mal épileptique en fonction de la thérapeutique. Éléments cliniques et électroencéphalographiques du pronostic)

P. VERGER, P. LOISEAU, M. L. ETCHEVERRY, and F. SERVILLE. Annales de pédiatrie [Ann. Pédiat.] 38, 183-191, Jan. 14, 1962. 1 fig., 17 refs.

An analysis is presented from the Centre Hospitalo-Universitaire, Bordeaux, of the results of treatment of 50 cases of petit mal with trimethadione (troxidone), usually combined with a barbiturate, and those features of the disorder, both clinical and electroencephalographic, which appeared to have prognostic significance in regard to response to this treatment are discussed in the light of other workers' experience. The authors found that the different clinical forms of the attacks, that is, whether "pure absences" or absences accompanied by automatism and/or myoclonus, all had the same prognosis, namely about 60% showed improvement with the drug. If the onset of attacks occurred late, however, or if the patient had akinetic attacks, the outlook was less satis-

factory. From the electroencephalographic (EEG) point of view the appearance of paroxysmal disturbances other than pure 3-per-second spike-and-wave tracings and the presence of certain interictal episodic disturbances lowered the expectation of benefit with "tri-dione" (troxidone).

The authors contrast these results with those obtained in 21 patients with petit mal treated with the derivative of succinimide, "zarontin". In this admittedly small group 17 of the 21 showed good or excellent results, thus confirming the efficacy of this drug already reported by other authors. Of great interest, however, was the finding that the clinical and EEG features which indicated the probability of a poor response to treatment with tridione no longer had this significance in the case of treatment with zarontin.

J. B. Stanton

1222. Learning and Retention by Monkeys with Epileptogenic Implants in Posterior Parietal Cortex. [In English]
J. S. STAMM and A. WARREN. Epilepsia [Epilepsia (Amst.)] 2, 229–242, Sept. [received Dec.], 1961. 5 figs., 7 refs.

At the Institute of Living, Hartford, Connecticut, epileptic lesions were produced bilaterally by the alumina gel method in the parietal region in 2 groups of monkeys in order to examine the effects of such lesions on learning and the retention of somatosensory tasks. One group of 5 animals was used in learning tasks of roughness discrimination and the other five in retention tasks of similar type. Alumina cream implantation was carried out after the first test was completed in the learning group and after the third series of tests in the retention group. The results showed that memory for learnit tasks was not impaired by the onset of epileptic discharges in the parietal areas, but that the acquisition of new discriminative tasks was considerably impaired.

The authors consider these findings in relation to the function of the parietal cortex.

J. B. Stanton

1223. Autonomic-psychic Experimental Epikepsy in the Cat Due to Insular and Circum-insular Lesions. [In English]

B. Blum and E. Liban. Epilepsia [Epilepsia (Amst.)] 2, 243-250, Sept. [received Dec.], 1961. 2 figs., 18 refs.

At the Weizmann Institute and the Kaplan Hospital, Rehovoth, Israel, the authors studied the characteristics of epileptic seizures produced in cats by tungstic acid gel lesions in the region of the insula. In most of the cats the seizures were predominantly of autonomic type, with manifestations of cardiac irregularity and respiratory and gastro-intestinal disturbance. Generalized convulsions were rare, but muscle twitchings restricted to the abdominal and chest musculature were seen and seizures could be precipitated in some cases by offering food to the animal. Behavioural disturbances were also seen mostly in cases where the lesions extended beyond the insula.

The authors discuss the significance of these findings in relation to the probable functions of the insula and surrounding areas and their relation to human epilepsy with similarly situated foci of origin.

J. B. Stanton

Psychiatry

1224. Contrasting Suicide Rates in Industrial Communities

E. STENGEL and N. G. COOK. *Journal of Mental Science* [J. ment. Sci.] 107, 1011-1019, Nov., 1961 [received Jan., 1962]. 14 refs.

The suicide rate in cities usually rises with the size of the population. The authors of this paper from the University of Sheffield examine the reasons for a high suicide rate in a comparatively small industrial town. They found that the mortality from suicide in Burnley was appreciably higher than that in Sheffield or Leeds, which are larger, though otherwise similar, towns. As a result of the closing of cotton mills Burnley has undergone a loss of young people, leaving an unduly high proportion of the elderly. By comparison, Leeds and Sheffield have been prosperous. There is also in Burnley a high proportion of widowed and divorced people, which is an index of social disorganization; the female population is relatively high. All these factors tend to produce a high suicide rate.

The proportion of coal-gas suicides in Burnley was above normal, and the use of this method, a very deadly one, can in itself lead to an increase in completed suicide.

The authors discuss the influence of physical illness and find a relationship between this and the suicide rate; they suggest that this relationship might be further explored.

Gavin Thurston

1225. Adolescent Violence and Homicide: Ego Disruption and the 6 and 14 Dysrhythmia

S. M. Woods. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 528-534, Dec., 1961. 31 refs.

Two case histories of adolescent murderers are presented. Psychological probing revealed that both had psychic conflicts which partially explained their superficially meaningless crimes. One had murdered a sister towards whom he had long harboured incestuous feelings. The other murdered an older female cousin, his guardian, on very trivial provocation, but it appeared that he hated her and had sadistic fantasies about her. However, both youths were intelligent and generally well behaved, and their murderous outbursts, which were carried out with repetitive ferocity, seemed utterly out of character. Both looked back on their crime with surprising blandness and lack of remorse.

On electroencephalographic examination both youths were found to have normal records apart from a positive dysrhythmia at 6 and at 14 c.p.s. This disorder, first reported by Gibbs and Gibbs (*Neurology* (*Minneap.*), 1951, 1, 136), affects adolescents of either sex, and accompanies a clinical syndrome which includes aggressive behaviour of an episodic, impulsive, and bizarre kind out of proportion to the precipitating factor, also recurrent attacks of pain and headache and of auto-

matic disturbances such as fever, nausea, flushing, or dizziness. There is no amnesia for the aggressive outbursts, but the urge is felt as compulsive, and subsequently the patient appears to be indifferent to what he has done, although in other connexions he retains appropriate feelings and seems generally a passive, conforming person.

D. J. West

1226. Sleep Deprivation: Transactional and Subjective Observations

G. O. Morris and M. T. Singer. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 453-461, Nov., 1961. 14 refs.

This paper, one of a series from the Walter Reed Army Institute of Research, Washington, D.C., which describe a 2-year investigation into the effects of sleep deprivation, reports the results in two groups of young soldiers: (1) a 72-hour sleep-deprived group composed of volunteer conscientious objectors with previous experience of such studies, and (2) a group deprived of sleep for 98 hours which came from a unit which had volunteered en masse. Despite some differences between these groups, their general pattern of reaction was similar. Each individual study involved 5 or 6 subjects and the same number of controls and lasted 11 days, the sleepdeprivation phase being preceded and followed by 3 or 4 days' observation. During the baseline period subjects were interviewed and performed psychological tests; two interviews were also carried out during the sleepless period.

The present report, based on 74 men, focuses especially on the interaction between subjects and that between subjects and staff. As the test period progressed the staff took a more active and personal interest in the subjects' welfare; however, toward the end of the studies, enthusiasm waned and subjects in the penultimate group tested were the only ones who needed to force the staff to keep them awake, a move which was associated with mutual resentment. During most of the studies the staff fostered denial of drowsiness by avoiding the topic; in addition, they anticipated and diverted potential aggressive outbursts, which had been a feature of other similar studies. Excessive laughter occurred as the period of sleep loss increased and it became "somewhat autistic". Anxiety was most apparent during the first day of sleep deprivation, but diminished thereafter and showed a shift from vague apprehension over loss of sleep to increasingly specific concern about the subjective effects of drowsiness. A variety of subjective experiences was reported; certain of these, such as weakness of the legs and sensations involving the head, later underwent elaboration, apparently as a result of "symptom contagion"; others, such as visual illusions, never spread in this way. It was observed that the most common method of dealing with the stress of sleep

deprivation was by denial of drowsiness. The 27 most intensely studied men could be divided into four significantly different groups: (1) those who admitted their difficulty in staying awake and who reported a minimum of other complaints and experiences; (2) those who avoided mentioning drowsiness but admitted associated changes; (3) a similar group who not only admitted but complained resentfully of these changes; and lastly (4) those who denied both drowsiness and other changes. Individual case reports illustrate each of these groups; in general, men with poorly integrated personalities were more often affected by loss of sleep and affected in a manner indicated by baseline projective tests and interviews. Nevertheless, the reactions of the staff and of his fellow subjects considerably influenced both the form and content of an individual's behaviour and experience Alan A. Black under these conditions.

1227. The Methacholine Response and Patient Improvement

G. A. Arneson. Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology [J. clin. exp. Psychopath.] 22, 215-222, Oct.—Dec., 1961 [received Feb., 1962]. 18 refs.

Many claims have been made for Funkenstein's test, which consists in recording the blood-pressure response to an injection of 10 mg. of methacholine chloride, one claim being that changes in the mental state of the patient are associated with definite changes in the blood-pressure response. The author of this paper from Louisiana State University School of Medicine and Charity Hospital of Louisiana, New Orleans, set out to examine this hypothesis. Tests were carried out on several occasions on 22 patients suffering from schizophrenic and depressive illnesses, and the changes in blood pressure were correlated with changes in the mental state of the patient. The results of the test are described and tabulated. Particular emphasis is placed on the finding that in patients showing a marked response to methacholine the prognosis was good, although changes in response were not necessarily correlated with improvement in the mental state. B. M. Davies

1228. Respiratory Variables in Response to a Pain-Fear Stimulus and in Experimental Asthma

R. C. Schiavi, M. Stein, and B. B. Sethi. Psychosomatic Medicine [Psychosom. Med.] 23, 485-492, Nov.-Dec., 1961. 6 figs., 14 refs.

The differences, if any, which exist between the respiratory changes in experimental asthma and those produced by a pain—fear stimulus were studied at the University of Pennsylvania School of Medicine, Philadelphia. The respiratory pattern in each of these syndromes is characterized by prolonged expiration or wheezing or both. Ten male guinea-pigs were placed in a body plethysmograph and given three electric shocks In another 17 guinea-pigs "experimental asthma" was produced by exposure to a process of sensitization to egg-white stimuli. The flow resistance and elastic distensibility (compliance) of the lungs of both groups of animals were then determined.

The electric shocks led to restlessness, tremor, piloerection, and screeching in the animals. There was a significant decrease in compliance but no change in flow resistance. This pattern appeared to be related to the actual screeching of the animals. In the experimental asthma group, there was a decrease of compliance with increased flow resistance. In both groups of animals, however, inspiration was shortened and expiration was prolonged.

The results indicate that the respiratory response to a pain-fear stimulus differs from that in experimental asthma. The airway resistance occurring in the latter is interpreted as evidence of bronchiolar obstruction, and it is suggested that asthma be defined in terms of bronchiolar as well as ventilatory indices.

A. Balfour Sclare

MENTAL DEFICIENCY

1229. Visual and Stereognostic Shape Recognition in Normal Children and Mongol and Non-mongol Imbeciles N. O'CONNOR and B. HERMELIN. Journal of Mental Deficiency Research [J. ment. Defic. Res.] 5, 63-66, Dec., 1961. 7 refs.

In this study of tactile and visual recognition of shapes, carried out at the Maudsley Hospital, Londón, the tasks given consisted in the verbal acknowledgment of recognition, both manually and visually, of 5 shapes based on Greek letters cut out in hardboard; each shape was presented initially for 10 seconds and again one minute later, in random order, together with 5 other shapes not previously presented on the first occasion. The subjects included four groups each of 24 persons of both sexes, namely, adult non-mongol imbeciles, adult mongol imbeciles, normal children, and normal adults.

It was found that the scores for stereognostic recognition of the shapes among non-mongoloid imbeciles were equal to those of normal subjects of the same chronological age, but that those of mongols were much lower than those of non-mongoloid imbeciles of the same I.Q. and age. On the other hand visual recognition scores were significantly highest among the normal adults, whereas in this respect the scores of normal children did not differ from those of imbeciles. The study thus confirmed that imbecile adults are superior to normal children in stereognostic shape recognition and that normal adults are superior to normal children in visual shape recognition.

G. de M. Rudolf

1230. Shape Perception and Reproduction in Normal Children and Mongol and Non-Mongol Imbeciles

B. HERMELIN and N. O'CONNOR. Journal of Mental Deficiency Research [J. ment. Defic. Res.] 5, 67-71, Dec., 1961. 1 fig., 7 refs.

In this further study [see Abstract 1229] 16 normal children aged 4½ to 5½ years and 16 mongol and 16 nonmongol subnormal patients of both sexes and of similar mental age to the normal children were tested for their ability to recognize, copy, and reproduce 4 simple directional and 4 simple proportional drawings which were each exposed for 10 seconds.

The scores for matching and recognition showed no significant difference as between the normal children, mongols, and non-mongols. Also there were no significant differences between the groups in their ability to match and recognize the directional drawings, as opposed to the proportional drawings. All groups obtained higher scores on matching than on recognizing designs. Mongols performed less well in the copying and reproducing than did the non-mongol imbeciles or the normal children. It is concluded that these results support previous findings that in tasks involving fine motor control mongols are inferior to non-mongols. They do not support findings which indicate that gross visual-perceptual defects necessarily occur in subjects with extensive malformation or damage of the brain.

G. de M. Rudolf

1231. Fluctuations in Intellectual Functioning Associated with Changing Sexual Maturity

K. Albert-Gasorek and J. M. Argrett. *Journal of Neuropsychiatry* [J. Neuropsychiat.] 3, 85-90, Dec., 1961. 1 fig., 5 refs.

This paper from Willowbrook State School, Staten Island, New York, is part of an interdisciplinary study of mental deficiency. The theory underlying the investigation is that physiological, endocrinological, psychological, biochemical, and behavioural events are interrelated. The present paper describes a controlled, double-blind investigation into the effect of specific hormone therapy on intellectual functioning.

Two groups of male adolescent mentally retarded patients matched for age, I.Q., and sexual immaturity were treated, one with chorionic gonadotrophic hormone and the other with a placebo. Psychological testing was given to all patients at various intervals before, during, and following treatment (which lasted 3 months). The patients receiving the hormone were shown to improve in intellectual functioning and their physical immaturity also improved. The change, though slight, was statistically significant at the 0·01 level and appeared to be related to changes in the ketosteroid excretion rate and amount of hormone given.

B. M. Davies

1232. An Analysis of 107 Non-communicating Children L. MINISKI and M. J. EVANS. *Journal of Mental Deficiency Research* [J. ment. Defic. Res.] 5, 77-97, Dec., 1961.

The authors present an analysis of 107 children who for one reason or another were unable to communicate and on this ground had been referred to Belmont Hospital, Sutton, Surrey. It was found that of these patients 38 were severely and 23 partially deaf and 46 were not deaf, of whom 8 however had no comprehension of speech. Of the 38 severely deaf 22 were ineducable, while 11 had I.Qs. of 50 to 70 and 5 an I.Q. of over 70. Of the 23 partially deaf 7 were considered ineducable, 8 were in the I.Q. range 50 to 70, and 8 in the range 70 to 96. Of those who were not deaf 31 were considered ineducable, in 3 the I.Q. was between 50 and 70, and in 5 between 75 and 95. Of 7 with normal comprehension of speech, one had an I.Q. of 65 and the others I.Qs. of between 80 and 110. Thus of 61 severely and partially

deaf children 48 had I.Qs. of less than 70, whereas of 46 who were not deaf only 4 showed these low I.Qs.

Of 12 children not mentally defective, 4 were severely and 6 partially deaf. A number of the children who were not deaf did not understand spoken language, while others did not understand sentences containing more than one idea; some did not even use gestures to express themselves. Many of the children who had never communicated were illegitimate, suffered from severe emotional disturbances usually due to rejection by the parents, and were insecure and severely deprived. The children investigated were in the age range 2 to 14 years. The authors state that children aged from 4 to 8 years are the most likely to benefit from suitable placement. A number of illustrative case histories are presented in detail.

It is planned to open an experimental school for 24 non-communicating, maladjusted, educable children, who will live in groups of 6 with a housemother and a teacher of the deaf, and the services of a psychiatrist and a psychologist will be available.

G. de M. Rudolf

1233. Psychologic and Neurologic Status of Diettreated Phenyiketonuric Children and Their Siblings P. W. Berman, F. K. Graham, P. L. Eichman, and H. A. Waisman. *Pediatrics [Pediatrics]* 28, 924–934, Dec., 1961. 1 fig., 30 refs.

The neurologic status and intelligence of 8 phenyl-ketonuric children treated with a phenylalanine-low diet were compared with that of 11 unaffected children and 3 untreated siblings. The mean intelligence of the treated children was significantly higher than that of their untreated siblings. This was true both for the 2 children given a special diet at 2 years of age and for those treated earlier, but the children treated before 6 months of age were significantly more intelligent than those treated at 2 years. The one child for whom treatment was begun at 1 year had an intelligence level within the range of the 5 who were treated earlier.

Although intelligence was significantly higher in treated than in untreated children, and this was especially marked in the children treated early, all treated children were significantly less intelligent than their unaffected siblings. The loss in intelligence probably cannot be ascribed to poor chemical control, as treated children maintained phenylalanine levels within the normal range throughout treatment, with occasional brief exceptions.

Neurologic findings paralleled the results of intelligence testing. There were no suggestive or positive findings among the unaffected children. Children treated early had some relatively minor findings, while children treated late and those who were untreated had a higher percentage and more marked signs of neurologic defect.

Results of the present study considered together with results from other investigations, indicate that intelligence level, in phenylketonuric children, is a decelerating function of age. If this is true, the brain may be especially susceptible to damage in the first few weeks and months of life, and treatment should be instituted as early as possible.—[Authors' summary.]

ALCOHOLISM

1234. Contribution to the Study of the Relation between Toxic and Metabolic Changes and the Psychopathological State in Chronic Alcoholism. (Contributo allo studio dei rapporti tra alterazioni tossico-metaboliche e stati psicopatologici indotti dall'alcoolismo cronico)

S. PROCACCINI and A. CHINI. Rassegna di neuropsichiatria [Rass. Neuropsichiat.] 15, 183-205, 1961. Bibliography.

After a short review of the literature on the metabolism of alcohol and the effects of chronic alcoholic poisoning. the authors report the results of a study of 50 alcoholic patients who were all inmates of the Asylum for the Criminal Insane, Aversa, and who had all been convicted of various crimes. After a full clinical examination of the physical and mental condition of these men the authors divided the patients into two groups on the basis of the mental state as follows: (1) 18 who were frankly psychotic, and (2) 32 whose mental state, while clearly abnormal, was not frankly psychotic. Laboratory tests and tests of liver function carried out in both groups included determination of the serum albumin:globulin ratio, electrophoresis of the serum proteins, various serum colloidal reactions, and the estimation (by Yamagata's method) of serum catalase activity.

Although abnormalities were found in these tests in both groups, and in particular a diminution in serum catalase activity, there was no correlation between the degree of liver damage (as assessed by the results of the liver function tests) and the severity of the mental disorder in these patients.

J. B. Stanton

1235. Suicide in Alcoholics

N. KESSEL and G. GROSSMAN. British Medical Journal [Brit. med. J.] 2, 1671–1672, Dec. 23, 1961. 11 refs.

It is well recognized that many alcoholics kill themselves, but there is little accurate information on the association between alcoholism and suicide. In this note from the Medical Research Council Unit for Research on the Epidemiology of Psychiatric Illness, University of Edinburgh, the incidence of suicide in 2 series of alcoholics is reported. The first consisted of 131 voluntary patients from the Maudsley Hospital, London, and the other of 87 patients who had for various reasons been committed for observation to St. Pancras Hospital, London. The criterion for inclusion was at least 5 years of excessive drinking.

Alcoholics are notoriously clusive, and where followup information was incomplete the quarterly death registers for England and Wales were searched, and a copy of the relevant death certificate purchased. Where necessary a transcript of inquest proceedings was also obtained. The authors point out that the results for suicide represent minima, as deaths occurring abroad or in Scotland or Northern Ireland would not be known.

No woman committed suicide. Of the men, 9 (8%) in the Maudsley Hospital series and 4 (7%) in the St. Pancras Hospital group killed themselves. Average ages were below those of suicides in general. During their stay in hospital alcoholics who ultimately com-

mitted suicide did not show any special features as compared with other alcoholics. The authors draw attention to the increased risk of suicide among alcoholics, but they regard the suggestion that suicide and alcoholism have a common underlying psychopathology as only speculative.

Gavin Thurston

AFFECTIVE DISORDERS

1236. Change and Constancy in the Clinical Picture of Depression. (Wandelbares und Bleibendes im Bild der Depression)

H. LENZ. Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete [Wien. Z. Nervenheilk.] 18, 321–356, 1961. 2 figs., 47 refs.

The author has reviewed the case records of all new in-patients admitted in every 5th year between 1903 and 1948 to a psychiatric hospital in Linz, Austria (783 in all) and all those showing a diagnosis of "endogenous depression" or "manic-depressive psychosis" (367 cases) were separated out, the object of the investigation being to see in what respect, if any, the psychopathology of the clinical picture of depression had altered during nearly half a century. The symptoms were classified as follows: (1) feelings of guilt and self-reproach; (2) feelings of detachment or of being "lost" or abandoned; (3) feelings of loss of ability to work or of poverty; (4) hypochondriasis; (5) suicidal ideas (including attempts and actual suicides); and (6) anxiety.

The male: female sex ratio of the patients had remained constant throughout at 1:3, and the age distribution also showed little variation. The symptoms of Type 1 showed a significant decrease when patients admitted in the period 1903 to 1933 were compared with those from 1938 onwards. The symptoms of Type 2 had increased slightly but significantly, while those of Types 3, 4, and 6 had remained unchanged. As regards suicidal ideas (Type 5) there was a steady and significant decrease over the period, particularly in the years following 1938. The author seeks the explanation for these changes in socio-cultural changes which have taken place during the first half of our century.

[These explanations, as well as the references to observations on psychopathological phenomena in other cultures, such as African or Indian, follow fashionable trends in cultural anthropology and, like these, are not entirely free from moralizing value judgments.]

J. Hoenig

1237. Dreams of Depressed Patients: Characteristic Themes in Manifest Content

A. T. Beck and C. H. WARD. Archives of General Psychiatry [Arch. gen. Psychiat.] 5, 462-467, Nov., 1961. 7 refs.

In an earlier study it was found that, compared with other psychiatric patients, those with depression more often dreamed of undergoing painful experiences, a characteristic which they share with non-depressed persons manifesting a masochistic life-pattern. For convenience, these dreams are also referred to as "masochistic", using the word in its popular rather than

psychoanalytic sense. The present study, carried out at the University of Pennsylvania School of Medicine and the Philadelphia General Hospital, extends these investigations.

A psychiatric and psychological examination was made of 287 unselected patients being admitted to the inpatient and out-patient departments. Depth of depression was assessed by the patients themselves on a "Depression Inventory" and by pairs of psychiatrists on a 4-point rating scale. Each patient was asked to describe his most recent dream and 228 of the patients could do so. The content of 218 of these dreams could be classified as either masochistic or not, according to predetermined criteria. When the Depression Inventory scores were ranked and divided into three equal groups representing moderate to severe depression, mild to moderate depression, and no depression, the number of masochistic dreams was significantly greater in the most depressed group and also in the combined depressed groups than in the non-depressed group. A similar association was found when the psychiatrists' ratings were similarly classified. Background factors such as age, sex, race, intelligence, and socio-economic status were shown to have no influence on the results.

The authors are explicit about their use of "depth" of depression rather than the primary diagnosis as a basis for classifying the depressions; this decision was taken because of the relatively low level of agreement that was obtained when using the A.P.A. Diagnostic Manual. They also stress that masochistic dreams are not only associated with a state of depression, but are also experienced by patients who have recovered from their depression as well as by individuals who have never had a depressive or other psychiatric illness. These latter are persons who appear to show masochistic trends in their general behaviour and it is possible that masochistic dreaming may be a correlate of predisposition to clinical depression. At the same time the authors acknowledge that caution is needed in interpreting dreams in relation to superficial similarities in waking behaviour unless there is considerable corroboration from other sources-[a point which is axicmatic among most Alan A. Black psychoanalysts.]

1238. A Clinical Analysis of the Effects of Tofranil in Depression. Longitudinal and Follow-up Studies. Treatment of Blood-relations. [In English]

J. Angst. Psychopharmacologia [Psychopharmacologia/ (Berl.)] 2, 381-407, 1961. 3 figs., bibliography.

This report from the University Psychiatric Clinic, Zürich, describes the results obtained with "tofranil" (imipramine) in the treatment of 200 patients, of whom 137 were suffering from endogenous depression. An important part of the investigation was a search among the patients' near relatives for those with psychotic illness and treating them also with imipramine. Of 105 in-patients (who formed the nucleus of the investigation) so treated 66% responded well or very well to the drug. Age, sex, constitution, pre-morbid personality, and family history did not appear to influence the effect of imipramine. It was found that daily doses of 200 mg. were

more effective than lower doses and that the occurrence of side-effects (that is, autonomic symptoms) favoured the prognosis. The best results were obtained in endogenous depression accompanied by inhibition and lack of drive. Longitudinal studies showed imipramine to be equal in efficacy to electric convulsion therapy, but that 20% of patients responded to only one of these 2 forms of therapy, while 10% were resistant to both.

From the study of the effect of imipramine on 14 blood relations of the patients it was concluded that those relations who were suffering from endogenous depression tended to respond to the drug in a similar direction (either positively or negatively) to the patients similarly treated. [It is unfortunate that this detailed study did not include a control group treated with a placebo.]

B. M. Davies

1239. Preliminary Pharmacological and Clinical Results with Desmethylimipramine (DMI) G 35020, a Metabolite of Impramine. [In English]

B. Brodie, P. Dick, P. Kielholz, W. Pöldinger, and W. Theobald. *Psychopharmacologia* [*Psychopharmacologia* (*Berl.*)] 2, 467–474, 1961. 9 refs.

This paper describes a joint study, carried out at five different centres in the U.S.A. and Switzerland, on the metabolites of imipramine ("tofranil"), of which several have been isolated. Of special note is the mono-methyl analogue desmethylimipramine (DMI). The pharmacology of this substance is described as well as its clinical effects. It is known that in man reserpine can produce a depressive illness, and that in animals a typical reserpine syndrome can be produced experimentally which can be blocked by antidepressant drugs. DMI has been shown also to have this effect. This action and its value in experimental work with antidepressant drugs are discussed. Clinically, DMI is more active than imipramine and appears to influence various types of depressive illness.

B. M. Davies

SCHIZOPHRENIA

1240. Cytology of the Cerebrospinal Fluid in Early Stages of Schizophrenia. [In English]

S. BEDNARSKI. Acta medica Polona [Acta med. pol.] 2, 353-367, 1961 [received Feb., 1962]. 15 figs., 19 refs.

From the Medical Academy, Lublin, Poland, the author reports the results of cytological examination of the cerebrospinal fluid (C.S.F.) of 25 schizophrenic patients (12 males aged 14 to 28 and 13 females aged 12 to 14 years) with duration of schizophrenia from one month to one year. Lumbar puncture was performed with the patient sitting. The small clot obtained after centrifugation was embedded in paraffin, sections 7 to $10~\mu$ in thickness cut, and these stained with haematoxylin and eosin and also with Giemsa and Romanowski stains. All the patients were receiving the normal hospital diet, without drugs.

The cells from the C.S.F. were well preserved. No erythrocytes were seen. In 16 cases neutrophil granulocytes were found in proportions varying from 1 to 11·1% (mean 4·2%). One eosinophil leucocyte was found in

each of 2 cases. Monocytes were found in 15 cases (proportions 1% to 20%, mean 6%). Mitosis was seen in 2 cases. Large lymphocytes predominated in 10 cases. In 16 of these patients the C.S.F. was then re-examined at varying periods after the completion of 3 to 5 weeks' treatment with "largactil" (chlorpromazine). Neutrophils now appeared in only 5 cases and monocytes in 8. Large lymphocytes still predominated in 10 cases. As controls, one hypochondriac and one neurasthenic patient were examined by the same technique. Small and large lymphocytes with a few monocytes were found in the C.S.F. of each of these subjects. The author points out that the finding of neutrophil leucocytes is very rare in C.S.F. from normal subjects so that their presence in proportions of up to 11.1% in these early schizophrenics is of importance.

No relationship between the clinical condition and the cytology was found, but it was noted that the number of neutrophils in the C.S.F. decreased when the patients had improved and gained insight following treatment.

G. de M. Rudolf .

1241. Children of Schlzophrenic Patients: Preliminary Observations on Early Development

D. E. Sobel. American Journal of Psychiatry [Amer. J. Psychiat.] 118, 512-517, Dec., 1961. 8 refs.

This paper describes an attempt to test the hypothesis that children whose parents are both schizophrenic develop emotional disorders in infancy and that the behaviour of the schizophrenic parents is at least partially responsible for this. Very strict criteria were adopted for the diagnosis of schizophrenia (and also for proved paternity) and it took the author 2 years to find 8 cases fulfilling the criteria among 65,000 patients in 7 State hospitals and 4 after-care clinics of the New York State Department of Mental Hygiene. Each of the 16 parents of the 8 infants had been in a mental hospital on at least one previous occasion.

By a fortunate chance the group was neatly divided, 4 of the infants going to foster homes after the neonatal period, and 4 being brought up by their schizophrenic parents. All 8 were visited every month and detailed observations made of their physical and emotional development and of the kind of interaction that existed between the infant and mother or foster-mother. The 4 infants in foster homes developed normally, but 3 of the infants brought up by their schizophrenic parents showed signs of chronic depression in the form of tearfulness, irritability, and sadness. These observations therefore confirmed the hypothesis.

The mothers of the 3 disturbed infants later suffered psychotic relapses and eventually had to be admitted to mental hospitals. All 3 were overtly depressed and engaged in little active play with the infants. It is suggested that the possible reasons for the emotional disturbance of the infants might be (1) a contagion of depressive emotions; (2) the absence of active stimulation by the mother; and (3) the absence of pleasurable reactions in the mother. The author also formed the impression that catatonic symptoms in the mother had a particularly harmful effect on the physical and emotional development of the infant. After the admission to hos-

pital of their mothers, the infants underwent "multiple separation experiences" (including 3 or 4 moves from one institution to another and in 2 cases short periods with their natural mother temporarily discharged from hospital) which affected them unfavourably. However, 2 of them were eventually placed in good foster homes for prolonged periods and have responded well with remarkable resiliency.

F. K. Taylor

1242. Social Treatment of Chronic Schizophrenia: a Comparative Survey of Three Mental Hospitals J. K. Wing and G. W. Brown. Journal of Mental

Science [J. ment. Sci.] 107, 847-861, Sept. [received Nov.], 1961. 2 figs., 2 refs.

This paper from the Social Psychiatry Research Unit of the Medical Research Council compares objective indices of the social care of chronic female schizophrenics in 3 large mental hospitals. All were aged under 60 and had been in-patients for more than 2 years. The diagnosis was checked by scrutiny of case notes and at interview, when the patient's symptoms were rated on a scale of severity. Altogether 273 patients (100 from each of Hospitals A and C and 73 from Hospital B) were investigated.

Hospital C differed from the others, and particularly from Hospital A, in the following respects. There was much less furniture per head. Patients spent a much higher proportion of time in the ward and in doing nothing and had far less organized occupation and leisure; only 30% left the ward at all (80% at A). 'A much higher proportion had no personal possessions, such as clothes, a comb, lipstick, or toothbrush, and the proportion of such possessions was much lower; at A 55% had scissors or nail-file (18% at B, 8% at C) and: 40% a mirror (11% at B, 4% at C). The attitude of nursing staff at A was far more optimistic—for instance, about such considerations as whether the patient could do useful work in hospital (76% at A, 52% at B, 26% at C), could bath without permission (75%, 42%, 37% could have matches (79%, 27%, 21%), could appreciate money, visit local shops, or be allowed out with a male patient. Hospital C rated much higher for ward restrictiveness based on such items as earliness of going to bed and locking the ward at night, and need for permission a for and freedom to use ward facilities and rooms.

No differences were found between A and C in the amount or frequency of sedatives and tranquillizers used; the amount per head at B was nearly double, and a higher proportion of patients were receiving them.

There were no significant differences between the hospitals in age distribution and the length of stay of the patients under investigation. Hospital A included a higher proportion of patients with fathers in professional and managerial occupations. Differences in attitude and management did not appear to be related to social-class origins of the patients.

The hospitals differed in the clinical state of the patients, a higher proportion at C being rated "/severely ill" (56% compared with 39% at B and 26% at A); in particular there was a much higher proportion of patients who were mute or spoke very little. The mean

rating for social withdrawal was much higher at C, but socially embarrassing behaviour was more common at B. A higher proportion at C were indifferent about leaving the hospital, but this was found to be related to duration of stay and poorer clinical condition. Patients at Hospital A showed least disturbance in verbal behaviour at interview, and in ward behaviour as rated by the staff.

The authors point out that they could find no differences in selection of cases or severity of illness on admission, nor was there evidence of a higher early discharge rate at C to account for the high proportion of clinically disturbed patients there; in fact, A had the highest annual discharge rate for schizophrenics. They conclude that there is good preliminary evidence that social conditions in a mental hospital do influence the mental state of schizophrenic patients. They suggest that "it will be necessary to show an improvement in patients in Hospital C, as the social regime there changes in order to confirm these results".

Christopher Wardle

1243. Histamine Metabolism by Schlzophrenic and Normal Subjects

Y. KOBAYASHI and H. FREEMAN. Journal of Neuropsychiatry [J. Neuropsychlat.] 3, 112-117, Dec., 1961. 10 refs.

It has been reported that allergic illnesses are uncommon in psychotic patients and also that such patients have a high tolerance of histamine. Such reports have given rise to various hypotheses about the relationship between histamine metabolism and mental illness.

This paper from the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts, describes an investigation in which minute quantities of histamine labelled with ¹⁴C were given to 12 chronically ill, disturbed, schizophrenic males and 7 normal controls. The histamine was given intradermally and urine specimens then collected. The various chemical derivatives of histamine were estimated and the results compared in the 2 groups. Both the schizophrenic and normal group had similar excretion patterns, indicating that schizophrenics can metabolize small amounts of intradermally injected histamine. However, statistical analysis showed that the groups differed in the distribution of the radioactivity among the 5 metabolites, although it did not indicate where this difference occurred.

B. M. Davies

1244. Experience in the Treatment of 16 Male Schizophrenics with Choriogonadotrophin and Depot Testosterone. (Erfahrungen bei Behandlung von 16 mannlichen Schizophrenen mit Choriongonadotropin/Depottestosteron)

K. DENGLER. Archio für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.] 202, 481-503, 1961. 21 refs.

At the Palatinate Nerve Clinic, Landeck, 16 male schizophrenic patients were treated with chorionic gonadotrophin and a depot preparation of testosterone. [These patients were highly selected, since only those with definite endocrine abnormalities were included.] Of the 12-patients who responded well to the treatment 10

were of leptosome body type and 2 of pyknic build, while of the 4 who did not respond 2 were leptosomes and 2 pyknic. Of the 12 patients who were hebephrenic 9 improved, whereas of 3 with paranoid schizophrenia only one showed a remission. The main endocrinal changes consisted in abnormal excretion of oestrogens and the production of gonadotrophin; abnormalities of corticoid excretion were less than previously reported by other workers. Thyroid activity was almost invariably increased. Psychopathologically the group was characterized by the marked sexual content of their hallucina simultaneous improvement in the endocrine and psychopathological abnormalities was noted in 7 of the patients.

J. Hoenig

1245. Experience with Promazine

N. H. RATHOD. American Journal of Psychiatry [Amer. J. Psychiat.] 118, 504-508, Dec., 1961. 30 refs.

The effect of promazine on the symptoms of 21 chronic female schizophrenics at Cane Hill Hospital, Coulsdon, Surrey, was investigated in a triple-blind trial. All the patients had been in hospital for at least 8 years, and their ages ranged from 37 to 67. All medication and physical treatment were stopped 3 to 4 weeks before the trial, and only occasionally were night sedatives given during it. The patients received either a placebo or 300 mg. of promazine daily by mouth for the first 3 weeks, these medicaments being reversed in the following 3 weeks. No one connected with the trial knew the nature of the medication being given at any one time.

No therapeutic effect of promazine could be observed either during the trial or subsequently when promazine medication was continued for another 10 to 12 weeks.

Further, the author reports that an equally negative result was obtained in an uncontrolled trial on 21 male patients (most of them schizophrenics) who had been in hospital for more than 15 months, while in another group of 24 male patients who had been suffering from various psychiatric disorders for less than 15 months improvement occurred in only 6. In discussion the difference between these negative findings and the positive results reported by other workers is attributed to the fact that "positive" results were obtained only in badly controlled investigations. Of 30 such trials reported in the literature, in only one was a "blind" procedure used and statistical evaluations carried out. Also little attention was generally paid to the environment in which the investigation was carried out, to ancillary treatments, and to ensuring an adequate duration of follow-up.

F. K. Taylor

1246. Comparison of the Effect of Thioridazine and Chlorpromazine on Chronic Schizophrenic Psychosis Using Double Blind Technique. [In English]

B. B. Syedsen, A. Faurbye, and P. Kristjansen. Psychopharmacologia [Psychopharmacologia (Berl.)] 2, 446–455, 1961. 12 refs.

The aim of this study, carried out at St. Hans Mental Hospital, Roskilde, Denmark, was to compare the effects of thioridazine ("melleril") and chlorpromazine on 61 chronic schizophrenic patients, 28 male and 33 female.

After an observation period of 3 weeks during which all drugs were withheld one or other of the active drugs was given for 12 weeks followed by the alternative drug for a further 12 weeks, a double-blind technique being used and observations being made throughout the trial by nurses and doctors. It was concluded that the drugs appeared to be of equal value in 27 patients, that 13 improved more while receiving thioridazine, and 12 were better with chlorpromazine. The incidence of side-effects was roughly similar with the two drugs, though thioridazine appeared less likely to cause tremor.

B. M. Davies

TREATMENT

1247. The Effect of Monoamine Oxidase Inhibitors on the Metabolism of Scrotonin and Epinephrine

A. FELDSTEIN, H. HOAGLAND, M. R. RIVERA, and H. FREEMAN. Journal of Neuropsychiatry [J. Neuropsychiat.] 3, 83-84, Dec., 1961. 7 refs.

This paper from the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts, reports investigations into a test for monoamine oxidase (MAO) levels in man which depends upon measuring the ratio of radioactive 5-hydroxyindoleacetic acid to total radioactivity in a specimen of urine collected after the administration of a dose of 5 μ c. of serotonin labelled with 14C. Certain MAO inhibitors have been shown to be of some value in certain depressive illnesses, yet their actual mode of action has never been clearly defined. The aim of the present study was to correlate the degree of MAO inhibition with the clinical effectiveness of the antidepressant drug, but the test proved unsatisfactory for this purpose. When the radioactive serotonin was given by mouth it was found that 'MAO inhibition occurred with drugs such as phenelzine and nialamide. If, however, the serotonin was given intravenously this inhibition was only slight. These findings raise various questions about the site of serotonin inhibition by these drugs. It is of interest that while intravenously administered serotonin was only slightly altered by MAO inhibitors, the metabolism of intravenously administered radioactive adrenaline was markedly altered.

[These studies are of great importance in elucidating the mode of action of this type of antidepressant drug.]

B. M. Davies

1248. Delirious Episodes during Psychiatric Pharmacotherapy. (Delirante Ablaufe unter psychiatrischer Pharmakotherapie)

H. HELMCHEN. Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.] 202, 395-411, 1961. 2 figs., bibliography.

Of 291 women who in the course of 2 years had been treated at the Psychiatric Clinic of the Free University, Berlin, with phenothiazine derivatives or similar drugs 17 (5.8%) developed 22 attacks of delirium. Although the ages of all patients in the series ranged from under 20 to over 90, with more than half under the age of 50, all the attacks of delirium occurred in patients aged over 50 years, and in 15 of the 17 only in patients with

organic psychoses, the two exceptions being one patient with schizophrenia and one with severe anankastic personality disorder; moreover in the former a concomitant organic cerebral lesion could not be definitely excluded. The drugs used were mainly "taxilan" (perazine) and "tofranil" (imipramine) in various dosage and given either singly or in combination. The dose of perazine being given at the onset of the attack of delirium was 200 to 900 mg. daily and of imipramine 200 to 350 mg. daily. The shortest period of treatment had been 16 days, but in most cases the duration was 2 to 4 months.

The attacks fell mainly into two types. (1) In one group of patients the onset was insidious, with predominantly subjective phenomena in the prodromal phase, during which the patient complained of tiredness, listlessness, and lack of energy; in this group the delirium itself came on later in the course of treatment, increased gradually night after night, was not florid, and on subsiding, left the patient tired and exhausted. (2) In the second. group onset was acute, with a short prodromal phase and the clinical picture dominated by objective motor signs and overactivity (gross tremor, rigidity, myoclonus, and involuntary rhythmic movements). In this type the delirium came on suddenly and in full force, with very florid symptoms such as visual and auditory hallucina, tions and gross disorientation, and when it passed left the patient, in many cases, refreshed. The underlying psychosis often showed some improvement and the delirium seemed to have had a therapeutic effect. The author discusses the significance of these observations in terms of cerebral physiology and localization, and ascribes the delirium to changes in the brain stem.

J. Hoenig

1249. The Action of Centrophenoxine against Fatigue. (L'action défatigante de la centrophénoxine)
P. Bugard. Presse médicale [Presse méd.] 69, 2295—2297, Nov. 25, 1961. 29 refs.

The author reviews the reputed properties of centrophenoxine ("lucidil"), a new psychotropic stimulant drug which improves alertness, but in many respects is unlike amphetamine. In the normal man it shows only placebo effects. It does not cause convulsions, though in large doses slow waves have been found to occur in the electroencephalogram. In addition, it has stimulant effects on the endocrino-metabolic system, seeming to function centrally, and has been shown to improve patients with panhypopituitarism. Its most remarkable use has been in patients with loss of consciousness due to organic, traumatic, or vascular causes.

The drug was tried at an endocrinological clinic in 45 patients complaining of chronic fatigue as a predominant symptom. The diagnostic categories of these patients included various psychoneurotic states, involutional depressive states, and other asthenic states of a reactive type. In the last two groups particularly, in which there were strong environmental factors, the drug proved helpful, seeming to reactivate and reharmonize the patient's life. The author concludes that its usefulness in such psychiatric patients enlarges the scope of a drug already accepted in other medical spheres.

J. S. Bearcroft

Paediatrics

1250. Difficulties in the Diagnosis of Congenital Abnormalities: Experience in a Study of the Effect of Rubella on Pregnancy

F. R. LOCK, H. B. GATLING, and H. B. WELLS. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 711-714, Nov. 18, 1961. 5 refs.

One hundred and seventy-six children were examined" twice by the same examiner at ages 4 to 12 months and a year later, at ages 16 to 25 months, for evidence of anomalous development following a pregnancy in which infection or exposure to rubella occurred. Of the anomalies found on the second examination 41% were not definitely recognized initially, 26% were totally unsuspected, and 15% were suspected but not proved on the first examination. The inadequacy of diagnostic criteria regarding mental status, visual acuity, auditory status, and cardiac murmurs in infancy is recognized. and careful parental guidance in doubtful cases is advocated. Dogmatic statements pertaining to the normal -mental status of an infant are to be condemned. Caution is important in interpreting data relative to congenital abnormalities from investigations that terminate with examination of children under one year of age.-[Authors' summary.]

[A fuller account of this survey has been published elsewhere (Lock et al., Amer. J. Obstet: Gynec., 1961; 81, 451).—EDITOR.]

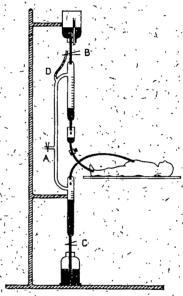
NEONATAL DISORDERS AND PREMATURITY

Exchange Transfusion by Continuous Drip Using Henerinised Blood

G. H. VALENTINE. Lancet [Lancet] 1, 10-13, Jan. 6, 1962.7 3 figs.

The idea behind the very slow exchange transfusion in the treatment of rhesus incompatibility recommended by the author is the more effective removal of the serum bilirubin than by the more usual technique of exchange transfusion. An attempt was originally made in 1949 to establish a balance-drip method of exchange transfusion by connecting the air inlet of the donor bottle to an empty bottle connected by air-tight tubes to an entry into the circulation so that for every drop of blood given an identical volume of blood would be removed, but the citrated blood caused clotting in the recipient system. After further trials a method has now been established using heparinized blood which has been successfully employed in 18 cases at the War Memorial Children's Hospital, London, Ontario, and which, according to the author, is easy to perform, requires no elaborate apparaalready packed and sterilized from a central supply.

depot. Once the drip has started it can be left to a good nurse to manage, care being taken to give heparin into the donor tube every 4 hours. From the author's experience 6 to 8 hours seems to be the best time in which. to achieve a satisfactory exchange of 80 ml. per lb. (176 ml. per kg.) body weight. This method appears to achieve a more effective removal of bilirubin for an equal amount of blood and to remove more bilirubin. from the body than the conventional method.



This paper aroused great interest when presented at a combined meeting of the British Paediatric Association and the Canadian Paediatric Society. However, further experience in the hands of other workers will be needed before paediatricians become convinced that they are justified in changing from what has proved to be an effective and successful method of treatment of rhesus incompatibility.]: David Morris

1252. On Real and Apparent External Bleeding in the

W. S. CRAIG. Archives of Disease in Childhood [Arch. .. Dis. Childh.] 36, 575-586, Dec., 1961. 19 refs.

In this communication from the University of Leeds the occurrence of external bleeding in 345 newborn infants seen over a period of 12 years is discussed. In regard to the site of the bleeding, this was gastrointestinal in 155 cases, cutaneous or subcutaneous in 96, and from the umbilical cord in 26, while haematuria tus, and needs only simple supervision. The apparatus occurred in 23 infants and haemoptysis in 18. Other used [see diagram] is described in detail. It is delivered causes of haemorrhage included trauma of anomalous superficial tissues, laceration during delivery and during

circumcision, and in 2 cases copious bleeding from the vagina. Trauma was responsible for the bleeding in 42 infants, infection in 20 cases, and developmental anomalies in 30. Disturbed coagulation of the blood was considered to be responsible in 106 cases. In 54 of the gastro-intestinal cases the bleeding was shown to be only apparent, being due to swallowed maternal blood. This can occur at any stage of labour and is especially likely after antepartum haemorrhage.

In the whole series there were 35 cases of traumatic cyanosis, and in 30 of these the mother had some illness. It is suggested that the maternal condition may be at least as significant as the mechanical circumstances of the birth in the appearance of this syndrome. The value of administration of vitamin K both prophylactically and as a curative agent in disorders of coagulation is discussed. The present series included 22 premature infants in whom there was bleeding in spite of treatment with vitamin K, and some of the other infants, who were 1 transferred from private nursing homes, had also received this vitamin. In the author's view it is doubtful whether vitamin K is of value either prophylactically or as treatment. The disturbed coagulation of the blood seems to be a temporary phase. The important factor in the treatment of the severe cases in this series was E. H. Johnson blood transfusion.

1253. Diagnosis of Kernicterus in the Neonatal Period R. VAN PRAAGH. Pediatrics [Pediatrics] 28, 870-876, Dec., 1961. 12 refs.

In a series of 882 infants with hemolytic disease of the newborn (erythroblastosis fetalis), 31 infants developed kernicterus. In the neonatal period the diagnosis of kernicterus was established firmly in 65%, remained uncertain in 19% and was not suspected in 16%. This diagnosis was established firmly in the neonatal period when spasticity was moderate to marked. The diagnosis of kernicterus remained uncertain when spasticity was mild and short-lived. This diagnosis was not suspected when spasticity was not observed.

Characteristically, a progression of three distinct clinical phases was observed in infants with kernicterus during the neonatal period. A fourth clinical phase appeared later in infancy. The first clinical phase was characterized by hypotonia, lethargy and a poor sucking reflex; the second by spasticity, opisthotonos and fever; the third by the diminution or disappearance of spasticity; and the fourth by the progressive appearance of the relatively permanent signs of post-kernicteric extrapyramidal cerebral palsy.

The hypotonia, lethargy and poor sucking reflex of the first phase of kernicterus appeared highly significant because of the great importance of this phase concerning the infant's neurologic prognosis. But these critical signs were nonspecific, being associated also with major pulmonary, cardiovascular and other central nervous system pathology in non-kernicteric infants with hemolytic disease. The spasticity of the second phase indicated with great accuracy that kernicterus had occurred in the first clinical phase. The diagnostic reliability of spasticity was not related to its intensity or durâtion.

A kernicterus-like syndrome related to hemorrhages within the basal ganglia was the only observed exception to the otherwise complete diagnostic reliability of spasticity. The true absence of any spasticity throughout the first week of life appeared to indicate with great reliability in the neonatal period that kernicterus had not occurred. The lessening or disappearance of spasticity in the third clinical phase erroneously led to diagnostic uncertainty in the neonatal period concerning the presence or absence of kernicterus.

It is hoped that accuracy in the diagnosis of the presence or absence of kernicterus in the neonatal period may be increased by an understanding of the three neonatal clinical phases, their cardinal signs, their progression and the diagnostic problems of each phase.—[Author's summary.]

1254. Serum Enzyme Activity in the Normal Newborn Infant

J. King and M. B. Morris. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 604-609, Dec., 1961. 8 figs., 18 refs.

Serum levels of bilirubin and of the enzymes glutamateoxalacetate transaminase (G.O.T.), glutamate-pyruvate transaminase (G.P.T.), lactate dehydrogenase (L.D.H.), and malate dehydrogenase (M.D.H.) were estimated in normal newborn infants at the North Lonsdale Hospital. Barrow in Furness. In all, 154 samples of cord blood and 41 specimens taken from a scalp vein during the first 9 days of life were examined, any specimen showing. haemolysis being discarded. Methods described previously by King were used for the serum enzyme estimations and a modification of the method of Malloy and Evelyn for determination of bilirubin. In cord-blood samples there was no relationship between bilirubin levels and those of any of the enzymes. The values for G.O.T., L.D.H., and M.D.H., were higher and showed a wider range than in the adult, while G.P.T. values were, lower and had a harrower range. During the first 9 days of life only the G.P.T. values showed any appreciable change, there being a small rise particularly after the 7th day which apparently bore some relationship to the fall in the serum bilirubin level, but the relatively small number of estimations précluded statistical analysis.

1255. Serum Enzyme Activity in Prematurity and in Haemolytic Disease of the Newborn

M. B. Morris and J. King. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 610-616, Dec., 1961. 7 figs., 5 refs.

In this further paper [see Abstract 1254] the authors discuss the activity of the serum enzymes in relation to neonatal jaundice, prematurity, and haemolytic disease of the newborn. Samples of blood were obtained from:

(1) 21 premature infants all of whom had more than minimal jaundice and 9 required an exchange transfusion for hyperbilirubinaemia; (2) 9 babies with anti-Rh haemolytic disease requiring exchange transfusion; and (3) 12 babies presumed to have anti-A haemolytic disease, of whom 5 required exchange transfusion. Serum

enzyme values higher than normal were found in most blood samples, especially after exchange transfusion, and particularly in those infants with anti-A haemolytic disease. The authors suggest that the figures obtained for glutamic—oxalacetic and glutamic—pyruvic transaminase indicate liver dysfunction, which in some cases appeared to have been made worse by exchange transfusion, possibly because of the use of Group-O blood containing immune anti-A: F. P. Hudson

CLINICAL PAEDIATRICS

1256. Amine Buffers in the Management of Acidosis: Study of Respiratory and Mixed Acidosis

S. KAPLAN, R. P. FOX, and L. C. CLARK JR. American Journal of Diseases of Children [Amer. J. Dis. Child.] 103, 4-9, Jan., 1962. 4 figs., 19 refs.

At the Children's Hospital, Cincinnati, 6 children suffering from acidosis were treated with an amine. buffer, tris - (hydroxymethyl) - aminomethane. THAM). The conditions responsible for the acidosis were hyaline membrane disease, pneumonia, bronchiolitis (2 cases), status asthmaticus, and open heart surgery. All except one of the patients were in a moribund state and the clinical condition was deteriorating in spite of conventional therapy. Five children recovered from their disease and remain well. The other child, who was undergoing open heart surgery, died of heart failure after 24 hours. The clinical course in these cases is outlined. Thus in a child with bronchiolitis respiratory distress continued in spite of tracheostomy and she developed convulsions and finally respiratory arrest. Artificial respiration was applied and tris given intravenously in 0.3 M solution. The blood pH rose, breathing became easier, there was profuse diuresis, and recovery was rapid. The total dose of tris was 12.7 g. The others had the same general reaction.

The factors of value in tris are: lack of toxicity, low molecular weight, stability, purity, solubility, availability in sterile form, and action on the renal tubules. Tris acts as an organic H ion acceptor, and apparently the unionized part readily enters the cells to act as an intracellular buffer. It is emphasized that tris does not replace conventional treatment of the cause of the acidosis.

E. H. Johnson,

1257. Obstruction to the Extrahepatic Fortal System in Childhood

S. SHALDON and S. SHERLOCK. Lancet [Lancet] 1, 63-68, Jan. 13, 1962. 2 figs., 28 refs.

In 1955 it was demonstrated that cavernomatous lesions of the portal vein were due to thrombosis and could cause extrahepatic portal venous obstruction. The authors of this paper from the Royal Free Hospital Medical School, London, describe 16 children in whom this syndrome occurred. Of the 16 children 9 had a history of neonatal umbilical sepsis; one of these had had an exchange transfusion, 2 had a history of staphylococcal pneumonia following umbilical sepsis, and one other had had a subphrenic abscess also following an

umbilical infection. The presenting symptoms and signs were chiefly splenomegaly and gastro-intestinal haemorrhage. Percutaneous splenic venography in 15 of the patients revealed obstruction at varying sites. In 13 the portal pressure was estimated and found to be raised. Ocsophageal varices were present in 12 of the 16 patients:

Conservative treatment was given in 5 cases, surgery being regarded as unwarranted or impracticable; it is considered likely that 3 of these 5 children may benefit from surgery later. Portacaval anastomosis was carried out in one child suffering from repeated gastro-intestinal haemorrhage, with permanent reduction in portal pressure. In the remaining 10 children various surgical procedures proved necessary. In all 16 children development has proceeded satisfactorily.

In a discussion the authors state that anaemia, if present, is due to blood loss from the gut and is corrected by iron therapy. If surgery is necessary portacaval anastomosis is the procedure of choice, but unless a venous shunt can be achieved satisfactorily conservative treatment should be given. The results of splenectomy have been disappointing.

J. G. Jamleson

1258. Ulcerative Colitis in Children: a Clinical, Psychological, and Social Follow-up Study. [In English]

T. ARAJÄRVI, R. PENTII, and M. AUKEE. Annales paediatriae Fenniae [Ann. Paediat. Fenn.] 7, 259-273, 1961. 1 fig., 22 refs.

The authors report from the University Children's Hospital, Helsinki, a follow-up study of 24 confirmed cases of ulcerative colitis in children aged under 2 to over 14 years (12 being between 2 and 5 years) at the time of onset who were treated during the years 1947 to 1956. An equal number of cases of rheumatic disease in children of similar ages treated during the same period were followed up as controls. Rheumatic disease was chosen for the purpose of control because these two diseases both tend to recur, to be protracted, and to affect children hitherto healthy, and both necessitate prolonged periods in hospital, these all being factors which exert similar psychological influences upon the child and his family.

The inquiry revealed the following facts: a familial occurrence of ulcerative colitis in 4 cases: a normal home in 16 cases: 5 of the patients were only children and 9 the eldest child in the family (the corresponding figures in the control group being 3 and 7 respectively); the social status (father's profession) of the families in the two groups was roughly similar; the age at onset of ulcerative colitis was somewhat lower than that of rheumatic disease. In the patients with ulcerative colitis faecal cultures were invariably negative, as was the Widal test in the 14 cases in which it was performed; anaemia was present in all cases while an interesting finding was an increased eosinophil count, suggesting a relationship between ulcerative colitis and the collagen diseases. The erythrocyte sedimentation rate was increased both in the acute stage and in recurrences in both groups, though to a greater degree in the rheumatic cases, but this was reversed at the time of follow-up, although there had been considerable improvement in both groups

since initial treatment. Measurement of the height of the patients with ulcerative colitis did not show any retardation of growth on the whole.

There were few intestinal complications of the ulcerative colitis; one patient died from severe intestinal haemorrhage on the way to hospital, but colectomy had to be performed in only one case. The intestinal complications included one case each of preternatural anus, rectal abscess, rectal prolapse, incipient rectal stricture, and anal fissure. Extra-intestinal complications were found more frequently, these including rheumatic arthritis and fever (6 cases), eczema (4), maxillary sinusitis (3), stomatitis (3), and 2 cases each of otitis media, furunculosis, pyelitis, and enuresis. The treatment of ulcerative colitis, in addition to the usual measures, included psychotherapy; of 7 patients so treated one with severe and 2 with moderately severe ulcerative colitis were cured. In general, patients with severe ulcerative colitis had a poor prognesis, only one of the 15 children severely affected having recovered, whereas 7 with mild or moderately severe disease were cured. Over-all the results of the follow-up study showed that 8 of the 24 children with ulcerative colitis were completely cured, but that 15 still had bloody stools or diarrhoea; of the 5 patients now over 18 years of age 3 are totally disabled: R. G. Mever

1259. The Prognosis of Chronic Ulcerative Colltis in Children

W. M. MICHENER, R. P. GAGE, W. G. SAUER, and G. B. STICKLER. New England Journal of Medicine [New Engl. J. Med.] 265, 1075-1079, Nov. 30, 1961. 6 refs.

The survival rate and the incidence of carcinoma of the colon in children in whom chronic ulcerative colitis was diagnosed before the age of 15 years were studied in 401 such patients seen at the Mayo Clinic between 1918 and 1959 inclusive. At the time of the study (January, 1961) 112 of the patients had died, death being directly related to the condition in 97—progression of the colitis in 57 and carcinoma of the large intestine in 40. Altogether 46 patients in the series had carcinoma of the colon, 6 being operated on and surviving up to 8 years afterwards. Careful analysis of the relevant data showed that death from carcinoma of the colon occurred 556 times more frequently in children with chronic ulcerative colitis than would be expected in the general child population.

A major surgical operation was performed on 85 of the 401 patients. Of 48 subjected to total colectomy with ileostomy 36 did not have cancer; 31 of these improved, one did not improve, and 4 died; the remaining 12 had cancer of the colon, 6 of whom (as stated above) were alive at the time of the study. Subtotal colectomy with ileostomy was carried out on 5 patients; 3 without cancer improved and 2 with carcinoma died. Palliative colostomy or ileostomy was performed on 32 patients (17 with carcinoma), 27 of whom died, including 16 with carcinoma. In the authors' view no conclusion can be reached concerning the place of surgery in these cases until more research into the problem has been carried out.

1260. Idiopathic Thrombocytopenic Purpura in Childhood, J. H. WALKER and W. WALKER. Archives of Disease in Childhood. [Arch. Dis. Childh.] 36, 649-657, Dec., 1961., 5 figs.; bibliography.

Between 1943 and 1958 114 children attending the University Department of Child Health, Newcastle upon Tyne, were diagnosed as suffering from idiopathic thrombocytopenic purpura. These patients form the basis of a detailed and largely retrospective clinical study of this condition. In 83 cases the disease was of the acute (self-limiting) type and in 31 the chronic form. The maximum age incidence occurred at 7 years, and there was no difference in sex incidence. Acute cases were most common in the spring and autumn. A history of a preceding infection was more frequent in those with the acute form. Drugs were not thought to be the cause of the condition, with one possible exception. In the acute cases the onset was usually, but not always, abrupt, whereas in most of the chronic cases it was insidious. Bleeding from the mucous membranes occurred in only one-third of the cases. Severe anaemia or enlargement of the spleen was rare. In all cases the platelet count was below 100,000 per c.mm. and in 81% it was below 40,000 per c.mm. Increased capillary fragility and prolonged bleeding time were found in most. but not all, of the patients. Clot retraction was impaired; in the 14 in whom this feature was studied. Platelet antibodies were found in 47 (75%) of the 64 patients so investigated; splenectomy did not influence this feature, nor could the course of the disease be forecast from the results of the antibody tests.

Of the 83 children with the acute form 3 died either of acute bleeding or following splenectomy. The others recovered, mostly within 4 months, but one spontaneousrecovery did not occur until after 21 years. Once the platelet count returned to normal the remission was always permanent. Of the 31 patients with chronic disease one died of cerebral haemorrhage 18 months " after the onset of symptoms. Of the others, 14 had only mild symptoms and splenectomy was not performed for this reason; these survive, although the platelet count remains low. In the remaining 16 splenectomy was performed because of persistent thrombocytopenia for over one year. The platelet count returned to normal in all cases, but relapse followed in 2 of the 16; 2 others developed repeated, serious infections following the operation., Corticosteroids were administered in 15 selected cases, but the results were not impressive.

A review of 58 certified deaths from idiopathic throm-bocytopenic purpura in children in England and Wales in 1955 and 1956 disclosed that only 12 cases were comparable with the authors' series; in 11 cases death was due to cerebral haemorrhage, usually in the early course of the disease and in spite of energetic treatment. 'A detailed review of the recent Anglo-American literature failed to disclose conclusive evidence that steroids are of real value in treatment, since most of the reported successes were obtained in those acute cases in which spontaneous remission was to be expected in any case. This does not exclude the use of corticosteroids for a short period at the beginning of an illness with acute onset. Splenectomy is dangerous in acute purpura but

safe in the chronic form. Post-splenectomy infections are not restricted to the youngest children, and not all cases are cured by splenectomy. This operation should not be undertaken if symptoms are minimal.

John Lorber

1261. Bronchiectasis: a Long-term Follow-up of Medical and Surgical Cases from Childhood

C. E. Field. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 587-603, Dec., 1961. 16 figs., 11 refs.

The outstanding feature found in a series of 225 cases of bronchiectasis commencing in childhood and followed up for 8 to 21 years was the improvement occurring at puberty and lasting usually through the teens.' This occurred equally in both surgically (121) and medically (104) treated cases. Bronchiectasis had usually arisen following an acute infection such as pneumonia or whooping-cough. Thereafter the child had had recurrent attacks of bronchitis, with persistently running nose and poor health. Between the ages of 6 and 12 there was usually slight improvement, but with the onset of puberty improvement was marked in many cases: Often the cough ceased, the child felt better, and activity was not impaired. This improvement seemed to occur quite apart from that due to surgical intervention or to treatment with antibiotics. The condition after the age of 20 years appeared to be stationary, but longer follow-up investigation is needed. During the last 6 years of the follow-up period 55% of the patients had had some intercurrent respiratory infection or asthma. "No cough" was reported in 33% of cases and "no sputum" in 44%. It was noted that the bronchiectatic patient was somewhat undersized and underweight compared with normal children of the same age.

General prognosis and the value of surgical intervention in different types of bronchiectasis is discussed. The fusiform and varicose types usually improve with the onset of puberty, whereas the sacculated and cystic forms of bronchiectasis appear to be irreversible and benefit from surgery. Asthma in a bronchiectatic patient offers a poor prognosis.

E. H. Johnson

1262. Clinical Experience in the Treatment of Oedematous Conditions in Childhood with a New Type of Longacting Diuretic. (Klinische Erfahrungen bei der Behandlung von Ödemkrankheiten im Kindesalter mit einem neuartigen Langzeitdiuretikum)

E. REIMOLD and H. RODECK. Archiv für Kinderheil-kunde [Arch. Kinderheilk.] 165, 113-125, Dec., 1961. 4 figs., 14 refs.

The authors report their results in 40 children aged from birth to 15 years who were admitted to the Paediatric Clinic of the Medical Academy, Düsseldorf, suffering from various diseases with or without manifest oedema, and who were treated with "hygroton" (chlorthalidone) in daily doses of 12.5 to 25 mg. for newborn infants, 25 to 50 mg. for older infants, and 50 mg. for children of school age. It was usually possible after 3 days to reduce the initial dose and to omit treatment altogether for periods of 24 hours from time to time. It was noted that the diuretic action of hygroton began only after

several hours, that it reached its maximum after 10 hours, and was maintained for 48 to 72 hours. The removal of oedema fluid was even, sodium and chlorides were excreted in almost equimolar proportions, and chloride acidosis did not occur. There was slight lowering of the serum potassium level in all cases, but this was easily corrected by giving fruit juices rich in potassium. In order to ensure that sufficient potassium is present for normal cardiac action when treatment with hygroton is protracted, the electrocardiogram should be regularly recorded and the serum electrolytes analysed.

The drug was well tolerated. There were no cases of impairment of hepatic, renal, gastro-intestinal, or bone marrow function or of allergic manifestations, and no evidence of any adverse effect on the blood pressure or blood sugar level was observed. Irritable and moody patients were often dramatically changed into normal, friendly, happy children with greatly improved appetites. It was found, however, that the newborn, especially those who were premature, and infants under 6 months of age were least benefited by hygroton, probably because of the immaturity of the renal tubules at this age. Thus in 6 cases of perinatal oedema the results were unsatisfactory; in 24 older children, however, with oedema of cardiac (8), hepatic (5), or renal (5) origin, or with oedema from allergy (3) or steroid therapy (3) they were good. The drug had little effect in 3 infants suffering from cerebral oedema and in 2 from hydrocephalus, but was of benefit in 4 older children with cerebral oedema and in one with hydrocephalus.

E. S. Wyder

1263. Clinical, Genetic and Electrocardiographic Studies in Childhood Muscular Dystrophy

A. SKYRING and V. A. McKusick. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 534-547, Nov., 1961. 7 figs., 37 refs.

The authors, from Johns Hopkins Hospital, Baltimore, describe the clinical picture, genetics, and electrocardiographic findings in 27 cases of muscular dystrophy arising in childhood. All of these were in males below the age of 20, and 23 presented the usual picture of pseudohypertrophic muscular dystrophy, which is usually inherited as a sex-linked recessive. In one family there were 4 affected males, and the pedigree demonstrates. undoubted sex-linked recessive inheritance. In 2 other families both a boy and a girl were affected. Usually it was thought that this inheritance was by autosomal recessive or autosomal dominant mechanisms. There was nothing in the clinical picture to differentiate between the sex-linked and the non-sex-linked forms of the disease, but electrocardiographic abnormalities occurred in 18 of the patients with the sex-linked form, while no such changes were seen in the other patients. In particular, changes were found in the QRS complexes of the right ventricular chest leads and especially in V1 and

[It is perhaps not generally known either by neurologists or cardiologists that muscular dystrophy may terminate with congestive heart failure resulting from pathological changes in the myocardium.]

Hugh Garland

ublic Health and Industrial Medicine

1264. Reinforcing Doses of Diphtheria Toxoid Absorbed through the Buccal Mucosa

W. C. COCKBURN, C. M. P. BRADSTREET, M. E. BAILEY, and J. UNGAR. British Medical Journal [Brit. med. J.] 2, 1754-1755, Dec. 30, 1961. 1 fig., 7 refs.

General practitioners, public health officers, and paediatricians, as well as parents and children, all have a practical interest in the reduction of the number of injections that must be given to complete a routine schedule of active immunization. This preliminary note from the Central Public Health Laboratory, Colindale, London, offers good hope that after the primary in ections booster doses of diphtheria toxoid may be satis-

factorily given by mouth.

The idea was introduced by Bousfield (Brit. med. J., 1945. 1. 833), who prescribed gelatin disks containing toxoid to be sucked daily for 7 days, and so obtained increases in the content of diphtheria antitoxin in the serum of persons previously immunized. The present authors have utilized subsequent knowledge to improve the method. They added hyaluronidase (which increases absorption through the buccal mucosa) to 1,500 Lf of purified diphtheria toxoid in 2 kinds of lozenge, prepared with different bases, which dissolved in the mouth in about one hour and 20 minutes respectively.

The results in 22 volunteers who had been previously immunized were similar with both types of lozenge. A substantial antitoxin response was observed, similar to that obtained by Edsall et al. (Amer. J. publ. Hlth, 1954, 44, 1537) after 2 injections of 1 Lf alum-absorbed toxoid at a 3-week interval to young adults, but less than that obtained when a third dose was given by the same workers. Nevertheless, only one of the 22 volunteers would probably have been Schick-positive after ingesting the lozenges. Studies in children aged 10 to 12 years are now in progress. [The results of these will be awaited with interest.] H. Stanley Banks

1265. Pollomyelitis Immune Status in Ecologically Diverse Populations, in Relation to Virus Spread, Clinical Incidence, and Virus Disappearance

R. S. PAFFENBARGER JR. and D. BODIAN. American Journal of Hygiene [Amer. J. Hyg.] 74, 311-325, Nov., 1961. 4 figs., 24 refs.

For this study, reported from the Johns Hopkins University. Baltimore, data on serum neutralizing antibody titres against poliomyelitis virus were obtained for communities in India, the United States, and Greenland. The endemic method of spread was demonstrated in Bombay, where poliomyelitis virus was "widely available", the disease being confined to the very young age groups. In Middletown, New York, poliomyelitis had occurred in epidemic form and the epidemics had resulted from either "the accumulation of disease-susceptible subjects" or entry of a virulent virus. In the isolated Greenland village of Narssak the infection showed a

periodic pattern of infection, for poliomyelitis virus had swept unnoticed through the population at least five times during the lifetime of the inhabitants. It is suggested that presumably similar effects could be produced in large communities by immunization with formalinized or live attenuated poliomyelitis virus vaccines.

A study of the epidemiological data in the State of Maryland for the period-1916 to 1955 showed that, compared with paralytic poliomyelitis, measles affected the younger-age groups. It appeared that measles spread primarily by transfer of the virus in respiratory secretions, but that the dominant method of transfer of poliomyelitis virus was contamination with faecal material. Where sanitary services were modern, as in Maryland and Middletown, spread of infective disease by faecal contamination occurred less frequently than among the relatively primitive populations of Bombay and Narssak. In Hidalgo County, Texas, virus spread was greater among the more primitive Latin-American population than among those who, like the Anglo-Americans, had modern sanitation and piped running water . A. Garland

INDUSTRIAL MEDICINE

1266. Emphysema and Pneumoconiosis. (Enfisema, e pneumoconiosi)

A. FERRARA. Medicina del lavoro [Med. d. Lavoro] 52, 420-443, June-July, 1961 [received Jan., 1962]. 17 figs., 58 refs. \.

The author, writing from the Institute of Pathological Anatomy and Histology of the University of Messina, first discusses the question of 2 types of morphologically similar emphysema. These are: (a) the perisclerotic circumscribed form; and (b) the diffuse type. The former is limited to a few alveoli surrounding the sclerotic focus, the latter extends to all the alveolar parenchyma not affected by the sclerosis.

As regards the relationship of the diffuse type to chronic emphysematous asthmatic bronchitis the author suggests that many writers agree that emphysema, as well as chronic bronchitis, frequently affects persons exposed to the risk of silicosis, but that the emphysematous lung changes are not related to the silicotic lesions or precisely to the nature of the substance worked with, but rather to unfavourable hygienic conditions at work. This raises difficult questions of compensation having regard to the definition of silicotic lesions in Italian law, which lays stress on the importance of detecting free silica in the fibrotic lesions. The problem is therefore to include the diffuse type of emphysema within the purview of the compensation laws: The author accepts, however, that a broncho-obliterative mechanism is at the root of nearly all cases of diffuse emphysema and states that most of the appearances of diffuse emphysema

seen in miners or those working in dusty industries are of strictly bronchogenic origin, the emphysema being centrilobular to start with and then extending outwards; this may be caused by mine dust even of low free silica content. The difficulty in determining the process when associated with fibrosis and also when the emphysema is associated with stenosis from outside of the bronchial rami is pointed out.

The author prefers the term "pneumoconiotic focal emphysema" (P.F.E.) to the "focal emphysema" of Gough, Hepplestone, and others, as the latter term can be applied to other lesions. In P.F.E. the bronchiolaralveolar junction and its surrounding elastic ring are affected, but whereas bronchiectasis affects the respiratory bronchioles, bronchiolar occlusion affects only the terminal bronchioles. This is especially evident in anthracosilicosis. As regards the causation of the bronchiolar occlusion, a contemporary affection of the bronchiolar mucosa is always found, especially in pumice workers where it is a true granulomatous and obliterating bronchitis, and is less evident in the other pneumoconioses. Oedema, spasm, increased viscosity of the bronchial mucus, and abundant desquamation all play a part in its formation. In the author's opinion the aerodynamic position proximal to the bronchiectatic bronchioles is important as here the negative pressure on inspiration is reduced to zero, producing stasis of the airflow and subsequent collapse and obliteration of the bronchioles proximal to the bronchiectasis. In other cases a valve system seems to form with air cysts under tension, thus leading to a vicious circle. If there is more septal fibrosis the emphysema will be of the lobular or bullous type, but not focal, while a very slow evolution of the pneumoconiotic lesion is also a necessary feature. Hence P.F.E. is almost specific to the pneumoconioses due to coal and other dusts of low free silica content. In non-sclerogenous pneumoconiosis the axial location of the tattooing due to coal dust situated at the final branches of the bronchioles before they widen and lead to the alveoli is a most prominent and exclusive fact. Focal emphysema is synonymous with bronchiolaremphysema and represents a midway path between bronchiectasis and lobular or vesicular emphysema.

- The author concludes that in pneumoconiosis there are: (a) emphysema of the diffuse lobular type with modest axial pneumoconiotic lesions' whose pathogenesis does not differ from the usual form due to asthmatic bronchitis; the bronchogenic factor is primary and is affected decisively by the ambient working conditions independently of the sclerogenous nature of the material worked with; diffuse lobular emphysema may represent the ultimate evolution of P.F.E.; (b) perisclerotic emphysema, either localized or diffuse, with associated nodular or linear sclerosis and the development of parenchymal changes, but not as a compensatory change; the bronchogenic factor is also demonstrable here; and (c) a special form of centrilobular circumscribed emphysema limited to the bronchioles of 1st, 2nd, and 3rd orders and strictly limited to pneumoconioses due to dusts with a low free silica content, with absence of pulmonary fibrosis; this is due to dystrophic injury to the musculo-elastic layer of the respira-

tory portion of the bronchiolus caused by deposition of the mineral and also by occlusive bronchiolitis. Hence P.F.E. represents the sum of the processes of penetration and fixation of dusts with low free silica content, especially coal. It runs a progressive course and so is compensatable. The bronchogenic factor is the linchpin of all 3 types.

W. K. Dunscombe

1267. Infective Pneumoconiosis Due to Anonymous Mycobacteria.

J. MARKS. British Medical Journal [Brit. med. J.] 2, 1332, Nov. 18, 1961. 5 refs.

The author of this paper from the Tuberculosis Reference Laboratory, Cardiff, describes recent experience of the examination of specimens of sputum from patients with progressive massive fibrosis (P.M.F.) of coalworkers. Up to 1960 sputum specimens were referred for examination only when there was clinical evidence of a tuberculous infection; since February, 1960, sputum has been examined in all cases of P.M.F. During the period-1953-9 anonymous mycobacteria were isolated from only 0.7% of cases, whereas in later years they were isolated from 2%. In a control series of patients without pneumoconiosis attending a chest clinic the isolation rate was 0.06%. The author suggests that the capacity to resist invasion by these relatively non-pathogenic bacterià may be impaired in pneumoconiosis and that the bacteria may play some part in the actiology of P.M.F. C. M. Fletcher

1268. The Significance of Radiographic "Calcification" in the Lungs of Coalworkers

J. P. LYONS and A. J. WATSON. Tubercle [Tubercle (Lond.)] 42, 457-469, 1961. 10 figs., 12 refs.

When disseminated nodular shadows of sufficient density to suggest calcification occur in radiographs of men with pneumoconiosis it is often assumed that these are due to tuberculosis rather than to the pneumoconiosis, particularly if this is coal-workers' pneumoconiosis. The authors, writing as members of the Glasgow Pneumoconiosis Medical Panel, report 6 coal-workers who showed radiographic opacities of this kind during life, but who at necropsy were found to have no definite evidence of tuberculosis. The shadows suggesting calcification were in 2 cases made by silicotic nodules, in one case by nodules of Caplan's syndrome, and in the remainder by calcification in infective nodules of coalworkers' pneumoconiosis. Although in the last-mentioned cases these "infective" nodules may have been tuberculous in origin, there was no evidence of classic pulmonary tuberculosis in any of these cases. The density of the radiographic shadows was not attributable. to the calcification, which was slight in all cases, but to the density of the collagenous fibrosis. The shadows were unlike those due to calcification in cases of tuberculosis in that they were more regular and more widely disseminated.

It is concluded that the type of calcification illustrated in this paper does not indicate tuberculosis and is entirely compatible with a diagnosis of coal-workers' pneumoconiosis.

C.M. Fletcher

1269. Clinical Features of Chronic Carbon Monoxide Poisoning. (Клиника жронической интокойкации окисью углерода)

M. A. Kovnackii. Гивиена Труда и Профессиональные Заболевания [Gig. Tr. prof. Zabolev.] 5, 25—30, Oct., 1961. 23 refs.

A review of the literature of chronic carbon monoxide (CO) poisoning showed that this may vary widely in its manifestations, affecting variously the nervous, endocrine, and cardiovascular systems. Preliminary investigations among industrial workers revealed that prolonged exposure to CO in low concentrations (0.04 mg. per litre of air) caused headache, vertigo, tinnitus, precordial pain, loss of memory, and muscle fatigue. The author found no clear correlation between the carboxyhaemoglobin (COHb) concentration in the blood and the clinical condition of the subjects. Those with a longer occupational history of exposure to CO had a lower COHb concentration in the blood, probably because of decreased affinity of haemoglobin for carbon monoxide. Vegetative dysfunction, as shown by changes in vascular tone, cerebrovascular crises, a coronary arterial pain syndrome, or any combination of these may occur. If protracted, these functional changes may lead to diffuse organic brain lesions.

The early changes in the heart were studied in 30 transport workers who had been exposed to CO for long periods. The R and S waves in the standard and chest leads on electrocardiography were broadened and the T wave diminished. The total blood cholesterol level was increased, and there was a marked rise in level of the cholesterol fraction not bound or only loosely bound to protein. It is stated that if these clinical signs are associated with a relative COHb concentration of 15% or more, they indicate a diagnosis of chronic carbon monoxide poisoning, and necessitate the transfer of the individual to other work where there is no risk of expessure to this gas.

Basil Hatgh

1270. The Effect of Continuous and Intermittent Exposure to Carbon Monoxide on Animals. (Некоторые данные о влияний на органиям животных окиси углерода в условиях непрерывного и интермитирующего воздействия)

I. D. GADASKINA, E. I. LJUBLINA, N. A. MINKINA, and M. L. RYLOVA. Гивиена Труда и Профессиональные Заболевания [Glg. Tr. prof. Zabolev.] 5, 13–18, Nov., 1961. 1 fig., 26 refs.

The effect of variation in the conditions of exposure to carbon monoxide (CO) was studied experimentally in rabbits, guinea-pigs, rats, and mice, which were exposed to CO either continuously or intermittently for 4 hours daily for 3 months. The "continuous" group of animals were exposed to a concentration of 0.036 mg per litre throughout the whole 4-hour period, while the "intermittent" group were exposed twice during the 4 hours to an initial concentration of 0.45 to 0.50 mg per litre for 6 or 7 minutes, which was then reduced to zero over 15 to 17 minutes; between exposures the latter animals breathed pure air. The mean total concentration of CO over the entire 4-hour period was the same for

both groups. Factors such as temperature and humidity, were adequately controlled.

The effects of poisoning were judged by the following factors. (1) In regard to carboxyhaemoglobin in the blood, animals in the "continuous" group showed none, while those in the "intermittent" group showed a carboxyhaemoglobin concentration of 15 to 16% at the peak exposure periods and none between exposures. (2) Changes in the time required for return of the respiration rate to normal after running on the treadmill were greater in the intermittent exposure group. A greater, effect was also observed in this group in regard to: (3)changes in motor activity (actography); (4) tests of i working capacity; (5) an orthostatic test; (6) summation of subthreshold impulses; and (7) tests of endocrine function (thyroid gland and adrenal cortex). Thus ineach case the tests revealed that the toxic effects of exposure to carbon monoxide were greater if the exposure was intermittent than if continuous. It is pointed out that this finding must be taken into consideration when a hazard from carbon monoxide poisoning exists...

Basil Haigh .

1271. Toxic Changes in the Cardiovascular System in Chronic Poisoning with Organic Mercury Compounds. (Динамика токсических изменений сердечно-сосудистой системы при хроинческой интоксикации органическими соединениями ртути)

N. S. LAŠČENKO. Гививна Труда и Профессиональные Заболевания [Gig. Tr. prof. Zabolev.] 5, 23-29, Nov., 1961. 2 figs., 5 refs.

The changes in the cardiovascular system were investigated in 34 persons after their withdrawal from contact with organic mercury compounds at various intervals over a period of 3 to 4 years. Each observation included a clinical examination and recording of the electrocardiogram (ECG) both at rest and after effort.

Clinically, the first evidence of mercury poisoning was dyspnoea, pain over the heart, and palpitations. It was noted that during the first months after cessation of exposure the precordial pain increased in severity. Disorders of cardiac rhythm (sinus bradycardia) developed; with muffling of the heart sounds and a functional apical systolic murmur. Hypotension was present at first, and not till one year after cessation of exposure to mercury did the arterial pressure return to normal or higher; at the same time the bradycardia gave way to a normal heart rate or even to tachycardia. The ECGs showed the following changes. The voltage of the P wave was lowered and the wave deformed or inverted, at first in one or more leads and later in all leads. The T wave was wide and low, later becoming higher and narrower, and after one year a spike was present; the voltage then fell, and giant T waves in the chest leads disappeared. The voltage of the QRS complex was lowered. The S-T interval was at first displaced, but became normally situated after one year. These changes are taken to indicate dystrophic changes in the myocardium and the conducting system of the heart. It is concluded that examinations to assess disability and fitness for work of persons at risk of exposure to mercury must include electrocardiography. .. Basil Haigh

Toxicology

1272. Use of an Osmotic Diuretic—THAM—in Treatment of Barbiturate Poisoning. Alkalinizing Action of Drug and Its Ability to Increase Elimination of Electrolytes in Urine Appears to Facilitate Clearance of Barbiturates

R. C. BALAGOT, H. TSUII, and M. S. SADOVE. *Journal of the American Medical Association* [J. Amer. med. Ass.] 178, 1000–1004, Dec. 9, 1961. 1 fig., 14 refs.

-After a general discussion of the treatment of barbiturate poisoning the authors, writing from the Department of Surgery of the University of Illinois, Chicago, advocate the use of 2-amino-2-hydroxymethyl-1:3propanediol (THAM) as an osmotic diuretic to increase the excretion of barbiturate. They describe a case in which it was given intravenously in a dosage of 300 mg. per kg. body weight in water (1,000 ml. containing 36.3 g. THAM with 1.75 g. sodium chloride and 0.37 g. potassium chloride) at the rate of 6 to 7 ml. per minute, 72 g. being given in 12 hours. Although the patient was comatose on admission, she was completely awake 20 hours after the start of therapy. Since THAM is also a buffer, the authors consider that the associated alkalinization of the blood and urine also helps in the elimination of the barbiturate. H. B. Stoner

1273. Calcium Disodium Edathamil Therapy of Lead Intoxication: the Significance of Amino-aciduria

B. F. Andrews. Archives of Environmental Health [Arch. environm. Hlth] 3, 563-567, Nov., 1961. 2 figs., 25 refs.

Three cases of lead poisoning in which excess aminoaciduria occurred only after the intravenous administration of calcium disodium edathamil (sodium calciumedetate) intravenously are reported from the Army Institute of Research and the Walter Reed General Hospital, Washington, D.C. Two of the patients were children with pica and were aged 17 and 23 months respectively. In the first case the urinary α -amino nitrogen value before treatment was 2-7 mg. per kg. body weight per day. (The normal range in early childhood is given as 2.0 to 4.0 mg. per kg. per day.) Sodium calciumedetate in a dosage of 75 mg. per kg. daily was administered in two 5-day courses, with an interval of 3 days between them. The urinary α -amino nitrogen value rose to 4.4 mg. per kg. per day and subsequently fell to 2,0 mg. per kg. per day. The second patient had 4 5-day courses of the chelating agent in a dosage of 60 mg. per kg. daily with intervals of up to one month between the treatments. The pretreatment value for urinary α-amino nitrogen excretion was 3·1 mg. per kg. per day. During the 4 courses it rose successively to 5.9, 10.7, 20.2, and 29.2 mg. per kg. per day. Sixty days after the last course it was still 6.3 mg. per kg. per day. In the third patient, an adult, the urinary α-amino nitrogen excretion before treatment was 2.0 mg. per kg. per day. (Normal values after early childhood are given as

1.0 to 2.0 mg, per kg, per day.) During a course of sodium calciumedetate (2.0 g, daily for 5 days) it rose to 3.9 mg, per kg, per day and afterwards fell to 1.3 mg, per kg, per day. Normal serum α -amino nitrogen values of 5.8 and 7.2 mg, per 100 ml, in the second patient and of 5.9 mg, per 100 ml, in the third were confirmed.

It is suggested that increased amino-aciduria, which in these cases occurred with treatment, represents altered proximal renal tubular function and that this could result from the chelate undergoing partial dissociation in the renal tubule, thus presenting the kidneys with a toxic concentration of lead for excretion. An alternative possibility considered is that the chelation of other trace metals might interfere with tubular function. It is noted that tubular lesions following the administration of sodium calciumedetate have been reported clinically and in experimental animals, and that these lesions resemble those resulting from heavy-metal poisoning, itself a known cause of amino-aciduria. The author recommends a more careful control of the dosage of sodium calciumedetate in the treatment of lead poisoning and increased intervals between doses if excess amino-aciduria persists after a 5-day course. J. J. Segall

1274. Phenacetin Takers Dead with Renal Failure: 27 Men and 3 Women. [In English]

O. NORDENFELT and N. RINGERTZ. Acta medica Scandinavica [Acta med. scand.] 170, 385-402, Oct., 1961. 2 figs., 25 refs.

The authors describe a series of 30 patients (27 male and 3 female) who died from uraemia in the Central County Hospital, Jönköping, Sweden: all had regularly consumed large amounts of phenacetin. The total consumption of the drug in the 10 to 20 years preceding death was at least 10 kg. The majority of the patients were industrial workers, 22 of the men coming from one factory employing 1,800 male workers [the nature of the work is not stated]. The authors state that the addiction is rife among these workers because they believe the drug increases their working ability. As much as 5 g, is taken daily, usually in powders containing 500 mg, of phenacetin, 500 mg, of phenazone, and 100 mg, of caffeine. This form of addiction is also common in various other parts of Europe.

The clinical features in these 30 cases and the morbid anatomy of the kidneys in 23 are described. The most frequent findings were contraction of the kidneys with chronic interstitial nephritis, tubular damage, and papillary necrosis. Ascending pyelonephritis was found in one-third of the cases. Although it is not clear how phenacetin damages the kidney, for the condition cannot be reproduced in animal experiments without simultaneous bacterial infection, the authors consider that their cases strongly support the view that heavy consumption of phenacetin-containing drugs over many years may lead to fatal uraemia. H. B. Stoner

Anaesthetics

1275. The Effects of Extradural Injection of Dilute Local Analessics

M. SWERDLOW and J. BROWN. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 642-647, Dec., 1961. 4 figs., 5 refs.

Extradural administration of 50-ml. volumes of low concentrations of lignocaine and 2-chloroprocaine results in very variable and unpredictable levels of analgesia and hypoaesthesia. Lignocaine provides analgesia of longer duration than that of corresponding concentrations of 2-chloroprocaine. Peripheral vasodilatation and hypotension were more marked with 2-chloroprocaine than with lignocaine at all concentrations and regardless of the levels of analgesia achieved.—[Authors' summary.]

1276. Guanethidine in Hypotensive Anaesthesia: Clinical Study in Patients Undergoing Microsurgery of the Middle Ear.

K. B. HOLLOWAY, F. HOLMES, and C. F. HIDER. British Journal of Anaesthesia [Brit. J. Anaesth.] 33, 648-654, Dec., 1961. 5 figs., 9 refs.

Ganglionic blockade may fail to provide a bloodless operating field in some patients, and in these cases inadequate hypotension is a frequent, and tachycardia a constant, feature. Guanethidine, a drug which produces hypotension with bradycardia, failed by itself in doses of 20 mg. to achieve a degree of hypotension sufficient to provide satisfactory wound ischaemia. In the 4 patients on whom guanethidine alone was tried operating conditions were poor, although in 2 of them subsequent injections of hexamethonium bromide resulted in adequate hypotension and a dry operating field. In 15 patients who exhibited tachycardia and inadequate or fluctuating hypotension following ganglionic blockade with hexamethonium bromide, the administration of guanethidine resulted in a fall in pulse rate and usually in a further fall in blood pressure. In these patients, previously poor operating conditions improved strikingly within 5 or 10 minutes following the injection of guanethidine.—[Authors' summary.]

1277. Methoxyflurane: a New Volatile Anaesthetic Agent, [In English]

N. Andersen and E. W. Andersen. Acta anaesthesiologica Scandinavica [Acta anaesth. scand.] 5, 179-189, 1961. 2 figs., 18 refs.

Methoxyflurane (2:2-dichloro-1:1-difluoroethyl methyl ether) was tried preliminarily in 55 patients undergoing various types of surgery. The purpose was to confirm that anaesthesia with methoxyflurane exhibits certain characteristic features which would suggest that this volatile agent may find a place in clinical anaesthesia.

Induction was found to be slow, and the sequence recommended is therefore barbiturate-succinylcholine induction. Emergence is also slow, and anaesthesia

should be interrupted well before the end of the surgical intervention. No special vaporiser was used and percentages of the agent offered to patients were calculated. on the basis of the chemical characteristics and on the specifications of the apparatus used (Dameca with Elam-Brown absorber). The present investigation involved studies of respiration (which is depressed), of brain activity (EEG [electroencephalogram] shows a definite pattern according to depth of anaesthesia), of circulation (ECG [electrocardiogram] is normal; blood pressure falls somewhat; pulse rate is remarkably constant), of blood chemistry, which is normal, and of liver function (transaminase), which showed depression within the usual limits. It appears that the myocardium is not sensitised to vasopressor drugs in patients who are under methoxyflurane anaesthesia.

The agent seems to be promising, but has the potential disadvantages of slow induction and slow emergence. Muscular relaxation is satisfactory already in the early stage of anaesthesia.

Methoxyflurane would most likely find a place as the main agent in prolonged operations and probably mainly in otology and neurosurgery.—[Authors' summary.]

1278. Experiences with a New Methyl-thiobarbiturate (B.137)

D. W. BARRON, J. W. DUNDEE, and R. KING. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 491-495, Sept.-Oct., 1961. 4 refs.

B.137, the methylated form of "inactin" ("inaktin"), has been subjected to clinical trial as an induction agent for intravenous anaesthesia, and compared with thiopental. The incidence of tremor and spontaneous involuntary muscle movements was so great as to more than outweigh any possible advantage which the drug might have as regards a more rapid recovery than thiopental.—[Authors' summary.]

1279. Combined Use of Halothane and Neuromuscular Blocking Agents for the Production of Surgical Relaxation

F. F. FOLDES, M. SOKOLL, and B. WOLFSON. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 629-639, Nov.-Dec., 1961, 15 refs.

The authors set out to determine which of the well-known neuromuscular blocking agents would produce surgical relaxation in conjunction with light halothane anaesthesia. A group of 219 patients undergoing abdominal surgery at Mercy Hospital, Pittsburgh, were premedicated with pentobarbitone, pethidine, and atropine, after which anaesthesia was maintained with nitrous oxide, oxygen, and halothane in half the patients, the remainder receiving thiopentone, nitrous oxide, and oxygen supplemented by a narcotic (alphaprodine or pethidine). In each of the two anaesthetic groups three

muscle relaxants were tested—namely, gallamine, suxamethonium, and toxiferene. The initial dose of gallamine or toxiferene was administered 3 to 5 minutes before the peritoneum was opened; suxamethonium was given by continuous intravenous infusion, which was started at this time.

With both anaesthetic techniques apnoea usually followed the initial dose of gallamine or toxiferene or occurred before the rate of the suxamethonium drip had been properly adjusted. The incidence and duration of apnoea were greatest with toxiferene and least with suxamethonium. At the end of the operation it was necessary to give neostigmine to 26% of the patients after halothane-gallamine administration, to 20% after thiopentone-gallamine, to 46% after halothane-toxiferene, and to 44.7% after thiopentone-toxiferene. The gallamine and toxiferene requirements in µg. per kg. body weight per minute were significantly lower in the patients who received halothane than in those given the thiopentone-narcotic combination. The mean duration of action of both first and second doses of gallamine was similar with the two anaesthetic techniques, as was the duration of action of the second dose of toxiferene. The duration of action of the first dose of toxiferene was, however, considerably longer in the thiopentone-narcotic group than in the halothane group.

The findings are detailed and discussed very fully.

Mark Swerdlow

1280. Postoperative Backache

E. M. Brown and D. S. Elman. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 683-685, Nov.-Dec., 1961. 8 refs.

The incidence of postoperative backache in 431 patients studied [at Sinai Hospital of Detroit, Michigan] was 20%: Neither the anesthetic technique nor the operative position significantly influenced the incidence of backache. The major factor involved in the occurrence of postoperative backache is the duration of time that the patient is subjected to postural stress by remaining immobile on the operating table.—[Authors' summary.]

1281. Effect of Thiopental Induction on Cardiac Output in Man

H. FLICKINGER, W. FRAIMOW, R. T. CATHCART, and T. F. NEALON JR. Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.] 40, 693-700, Nov.-Dec., 1961. 8 figs., 12 refs.

The effect of thiopentone induction on cardiac output was studied at Jefferson Medical College, Philadelphia, in 12 adult patients (average age 51 years) before intubation, full anaesthesia, and surgery. The patients were premedicated subcutaneously one hour beforehand with morphine or pethidine plus atropine or scopolamine. On arrival in the anaesthetic room each patient was kept until he was considered to be in a "steady state", when pulse, blood pressure, and two measurements of cardiac output were recorded. Multiple injections of 2% thiopentone were then given intravenously over a period of 30 to 120 seconds until the patient's lid reflex was lost, at which time the post-induction cardiac output was

determined and the pulse and blood pressure recorded. The total dose of thiopentone ranged from 100 to 400 mg. Cardiac output was measured by a modified dye-dilution technique, which is briefly described.

A fall in cardiac output of more than 15% was observed in 10 patients; in one patient there was no change and in one there was an increase in cardiac output of 14%. A fall in the mean arterial pressure occurred in 10 of the 12 patients, the average fall being 9.5 mm. Hg. In most patients the blood-pressure changes were not accompanied by any significant alterations in the pulse rate. In the 10 patients who showed a fall in cardiac output there was an accompanying increase in peripheral resistance. The results are discussed at some length.

[It may be asked why younger patients were not chosen.]

Mark Swerdlow

1282. Frequency of Cardiac Arrest Associated with Anesthesia in Infants and Children

H. RACKOW, E. SALANITRE, and L. T. GREEN. *Pediatrics* [*Pediatrics*] 28, 697–704, Nov., 1961. 9 refs.

This article from the Columbia-Presbyterian Medical Center, New York, discusses the frequency of cardiac arrest due to anaesthesia in infants and children up to and including the age of 12 years for the 10-year period 1947-56. This is defined as the number of cases of cardiac arrest in proportion to the number of anaesthetics given, anaesthesia being implicated if it was directly responsible or an important contributory factor. A table showing the type of surgery performed is given, approximately 50% of the operations being on the eye, ear, nose, or throat. Infants less than 1 year of age constituted 12.5% of all children operated upon and 2.6% of all patients, including adults, to whom anaesthetics were given.

In infants up to one year there were 6 cases of cardiac arrest due to anaesthesia and one to causes unknown among 4,308 anaesthetics, a total incidence of 1:615. In children aged 1 to 12 years there were 13 cases of cardiac arrest due to anaesthesia and 5 to causes unknown. in 30,191 cases of anaesthesia (1:1,677). These two groups combined gave a frequency of arrest of 25 in 34,499 anaesthetics (1:1,380). During the same period in adults (over 13 years of age) there were 51 cases of arrest in 131,668 anaesthetics (1:2,580). The recovery rates, complete and partial, were approximately 32% for children and 50% for adults. The frequency of cardiac arrest due to known causes and the combined frequency due to known and unknown causes (not including the patient's disease) represent minimum and maximum estimates, the true frequency lying somewhere between. Thus in infants up to 1 year the incidence of cardiac arrest during anaesthesia was significantly higher than in children (1 to 12 years) or adults (13 years and over). rate for all children was also significantly higher than that for adults, but not the rate for children of 1 to 12' years. The results of other workers are cited but these are not strictly comparable. The higher frequency of cardiac arrest found in infants than in older children and adults could not be correlated with any factor in the management of anaesthesia. Raymond Vale

Radiology

1283. Two Further Cases of Acute Radiation Sickness in Man. (Еще два случая острой лучевой болевни у неповека)

G. D. Bassogoi Ov' and A. K. Gus' коva. Клиническая Медицина [Klin. Med. (Mosk.)] 39, 43-56, Nov., 1961. 15 refs.

Having reported a number of cases of acute radiation sickness in 1955, the authors here describe the results of a very detailed investigation of 2 further patients who were subjected to severe irradiation during a laboratory accident, the total doses of whole-body irradiation received being 670 and 320 r. respectively. Both were young women, aged 19 and 24 respectively, and both, but especially the first, were extremely ill. Their progress was observed for nearly 4 years.

The disease could be divided into 4 stages. The first, lasting about 2 days, was due to the direct action of radiation on the tissues and the nervous regulating centres; it was characterized by weakness, nausea, and vomiting. This last might be extremely persistent. This stage was marked by tenderness of the abdomen, icterus, low blood pressure, diminished atrio-ventricular conductivity as shown by the electrocardiogram, neutrophil leucocytosis, lymphopenia, thrombocytopenia, and billirubinaemia. In one case there were increased tendon reflexes in the arm, with some diminution of the abdominal and Achilles reflexes. No free hydrochloric acid was obtained from the vomit. There was hyperaemia of the face and limbs.

The second stage was marked by some improvement in the patient's general condition, but aphthous stomatitis developed. Bone-marrow puncture revealed serious damage to the more primitive elements, haemocytoblasts; erythroblasts, and myeloblasts having almost disappeared. Localized neurological abnormalities, such as mystagmus, asymmetry of tendon and abdominal reflexes, and unequal perception of vibration on the 2 sides, were observed. The neutrophil leucocytosis was replaced by leucopenia and there was a severe fall in haemoglobin content and crythrocyte count of the peripheral blood. There was cerebral disturbance revealed in the electroencephalogram by the presence of theta and delta waves. Marrow puncture showed no signs of regeneration at the end of this stage.

The third stage, beginning on the 16th day, was marked by the onset of severe alopecia and skin changes (oedema, blistering). The patients felt worse, appetite was diminished, and there was a loss of weight and pyrexia. There were, strange to say, no haemorrhagic manifestations in the more heavily irradiated patient; but the other had numerous petechiae (which may, however, have been due to her being sensitive to penicillin). There was great lability of the pulse rate (50 to 70 per minute on lying down, 100 to 120 on standing). Anaemia was more pronounced than in the second stage, and marrow puncture

showed complete inactivity of the haematopoietic cells, absence of myeloblasts and megakaryocytes, and very few erythroblasts. Lymphocytes, however; were tending to increase. The destruction of primitive cells in the first stage was now expressing itself in an almost complete absence of the intermediate forms. By the 26th day, however, the myelograms began to reveal some return of haematopoietic activity.

The fourth stage was marked by slow recovery of cardiac, nervous, and haematopoietic function, and the patients began to feel better and to gain weight. In one bilateral cataract developed 3 years after the accident.

The treatment employed was complex. Immediately after admission to hospital both patients received gastric layage, which definitely improved their symptoms. Soon after, 650 ml. of blood was removed and replaced with 600 ml, of whole blood to which had been added 60 ml. of 40% glucose solution, 10 ml. of 10% potassium chloride solution, 10 ml. of 10% ascorbic acid solution. and 10 ml. of 0.5% procaine solution. They were confined to bed and put on a diet of junket, fruit, and vegetable juices. They received antibiotics—at first streptomycin and penicillin and later wider-spectrum preparations such as oxytetracycline and chlortetracycline. For the stomatitis they received gramicidin and nitrofurázone and for the skin lesions soothing lotions and ointments of neutral fats. Frequent transfusions of blood alternating with plasma were given. The authors consider that the value of marrow transplantation in the later stages is over-rated, but that its earlier use may be useful. The main object of treatment is to maintain the patient and ward off infection until regeneration of his bone marrow takes place. Supervision must continue for at least 4 years after apparent recovery.

[A most instructive article.] L. Firman-Edwards

RADIODIAGNOSIS

1284. Radiological Investigation of the Small Intestine W. G. Scott-Harden, H. A. R. Hamilton, and S. McC. Smith. Gut [Gut] 2, 316–322, Dec., 1961. 9 figs,, 5 refs.

The routine barium follow-through examination has proved unsatisfactory in the diagnosis of abnormalities of the small bowel. The filling of the small intestine is controlled by the rate of delivery through the pylorus, which is unpredictable. The follow-through procedure tends to produce irregular filling and any irritability of the bowel further complicates the picture by producing floculation and fragmentation of the barium column. A small lesion may be obscured by overlapping coils. The barium column is propelled forwards by peristaltic activity, the maximum diameter of the lumen being controlled by the tone prevailing at the moment. An early

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lesion causing minimum constriction will not be visible if the constriction has not yet reduced the lumen below that permitted by the tone prevailing. Failure to demonstrate diverticula and fistulae may be due to the maintenance of tone and peristaltic activity preventing the entry of barium into them during the passage of a bolus. The definition of adhesion may also cause difficulty; here the diagnosis depends on the ability to test the mobility of each segment. All these factors limit the value of the ingested barium meal as a diagnostic procedure. A successful technique must be one which will be independent of peristaltic activity and prevailing tone; at the same time the obscuring of bowel segments by overlapping must be avoided. If possible a double contrast method should be available.

The technique of barium small bowel enema, which has been described by other workers, has not found favour because of the technical difficulties and the fact that it does not overcome the disadvantage of overlapping coils. A simple small bowel enema technique (previously described by one of the authors) has been used as a standard procedure for 6 years at the Cumberland Infirmary, Carlisle. In this technique 20 ml. of "microtrast" is diluted with 80 ml. of water; onward progress of the contrast column is achieved by the subsequent injection of tap water and the barium left behind adhering to the mucosa serves to give a double contrast.

John H. L. Conway-Hughes

1285. The Diagnostic Accuracy of Upper Gastrointestinal Radiologic Studies. [Review Article]
R. N. COOLEY. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 628-650, Nov., 1961. Bibliography.

1286. Pelvo-spondylltis in Rheumatold Arthritis W. Martel and I. F. Duff. Radiology [Radiology] 77, 744-756, Nov., 1961. 14 figs., 35 refs.

This report from the University of Michigan compares and contrasts the radiological findings in the spine and pelvis in rheumatoid arthritis and ankylosing spondylius, 40 patients with advanced disease of each type being examined. There was a much greater proportion of females among the patients with rheumatoid arthritis (26) than among those with ankylosing spondylitis (7) and the average age was somewhat higher, though the duration of disease in the 2vgroups was comparable.

Sacro-iliac lesions, found in all the cases of ankylosing spondylitis, were present in 13 of the cases of rheumatoid arthritis. The latter differed in that the subchondral erosions were more clearly defined and showed less reactive sclerosis. Moreover, they were almost entirely confined to the true sacro-iliac articulations, which are shown by a radiograph of any anatomical specimen with a metallic marker outlining the articular surface to be restricted to the lower two-thirds of the joint, the upper third being the site of ligamentous attachments. This upper third was only once involved in the cases of rheumatoid arthritis, although in the late stages of that disease 4 showed fusion of the lower part of the joint. This was comparable to the fusion seen in the late stages

of ankylosing spondylitis, but in this condition involvement of the dorso-lumbar spine was generally present, a feature not seen in rheumatoid arthritis.

Erosions of the symphysis pubis and ischial tuberosities, again more clearly demarcated and with less reactive sclerosis, developed in only 3 and 5 cases respectively in the group with rheumatoid arthritis compared with 14 and 19 in the spondylitic group.

Spinal changes in rheumatoid arthritis were virtually absent in the dorso-lumbar region, whereas more than half the cases of ankylosing spondylitis showed the classic signs of vertebral squaring, apophysial joint ankylosis, and decreased disk height. In the cervical spine, on the other hand, vertebral subluxations and erosions affected half the cases of rheumatoid arthritis and were uncommon in ankylosing spondylitis.

R.O. Murray

RADIOTHERAPY

1287. Irradiation of Cerebral Astrocytomata under Whole-body Hypothermia

M. Bloch, H. J. G. Bloom, J. Penman, and L. Walsh. Lancet [Lancet] 2, 906-909, Oct. 21, 1961. 1 fig., 20 refs.

The sensitivity of tissues to x-irradiation is increased with an increase in available oxygen. Reduction in temperature, although decreasing the consumption of oxygen, increases the amount dissolved in the tissues.

At the Royal Marsden Hospital, London, 14 cases of cerebral glioblastoma multiforme (astrocytoma) Grades III and IV have been treated by irradiation under mild hypothermia (30 to 33° C.). Clinical effects not observed at normal temperatures with a comparable dose resulted in the signs of an acute cerebral reaction (dilated pupils, paresis, and other signs). These were reversible by the administration of urea solution through a Ryle's tube and were probably due to cerebral oedema. Although cerebral oedema is poorly tolérated owing to the harmful effects of raised intracranial pressure and the total dose of cerebral irradiation under hypothermia thereby severely restricted, this limitation may not apply to the treatment of tumours at other sites of the body, where a higher dose may be achieved and better results obtained. However, in view of the unexpectedly severe reactions reported here, caution is recommended.

L. A. Elson

1288. X-ray Sieve Therapy of Bronchial Carcinoma B. Jolles. British Journal of Cancer [Brit. J. Cancer] 15, 460-467, Sept., 1961. 3 figs., 12 refs.

In the author's opinion, if bronchial carcinoma is to be treated by x-irradiation, sieve therapy has distinct advantages over conventional methods. Large volumes may be treated, and skin damage and lung fibrosis are reduced. During the period 1954–57 sieve therapy was employed for 117 out of 140 patients treated with x rays at Northampton and for 78 out of 212 patients so treated at Oxford. The object of this paper is to compare the results with those in cases treated with conventional irradiation at Oxford and Reading, and with collected figures from other centres. (The 3 towns referred to are

included in the Oxford Regional Hospital Board Area.) 1290. High Voltage X-ray Therapy as a Primary Method The openings in the lead sieve were 0.5 to 10 cm. in diameter, the total area of the openings being preferably-50% of that of the sieve. Kilovoltage was 200 to 250, and the H.V.L. 2 mm. of copper. The daily dose varied between 500 and 800 r. (occasionally 1,000 r.) through, one or 2 fields, the duration of treatment being 4 to 6 weeks, with occasionally a second course after 6 to 8 weeks. The tumour dose, assessed as the average between the dose under the open area and that under the shielded portion, was 2,500 to 4,500 r.

Tables are given showing that, whereas after conventional x-ray therapy 30% of patients survived at 6 months, 9% at 12 months, and 3% at 24 months, the corresponding figures after sieve therapy were 52%, 23%, and 4%. For 4 other centres the figures for conventional methods are given as: 6 months, 28.5%; 12 months, 9.5%; 24 months, 3%. The author claims that with sieve therapy the radiation effects are less than with conventional x-ray therapy and the period of life remaining to the patient is therefore more bearable.

: E. Stanley Lee

1289. Supervoltage Radiotherapy for Cancers of the Uterine Cervix

G. H. FLETCHER. British Journal of Radiology [Brit. J. Radiol.] 35, 5-17, Jan., 1962. 3 figs., 17 refs.

This paper describes the results of treating cervical carcinoma with radiation from the 22-MeV. betatron at M. D. Anderson Hospital and Tumor Institute, Houston, Texas. For the purposes of treatment Stage II of the international classification is subdivided into Stage Πa , in which the disease is limited to the upper two-thirds of the vagina and/or there is minimal involvement of the parametria, and Stage IIb, where there is still tumour-free space but the disease extends almost to the pelvic wall or there is a barrel-shaped uterus. Stage III is subdivided into Stage IIIa, when only one pelvic wall is involved, and Stage IIIb, when both pelvic walls or one pelvic wall and lower third of the vagina are involved.

The treatment policy in Stage I and IIa carcinoma is 2 to 4 radium insertions giving 8,000 to 12,000 mg.-hours in 2½ to 4 weeks followed by 3,000 to 4,000 rads to para-'metria and pelvic walls. Stage Πb is treated by 4,000: rads pelvic dose in 4 weeks followed by 5,500 to 6,500/ mg.-hours in 2 insertions in 2 weeks. Stage IIIa has 6,000 rads pelvic dose in 6 weeks followed by 4,000 to 5,000 mg.-hours in one insertion. Stages IIIb and IV have 7,000 rads pelvic dose in 7 weeks, with occasionally additional 2,000 to 3,000 mg.-hours in one insertion. The external radiation was provided by the betatron. The techniques are described in detail.

Adenocarcinoma of the cervix is treated by radium therapy followed by hysterectomy. Lymph-node dissections were performed on a few patients, and involved pelvic nodes were found in one out of 41 Stage-I cases, 5 out of 64 Stage-IIa cases, and 12 out of 59 Stage-IIb cases.

The 5-year survivals were: Stage I, 93%; Stage IIa, 83%; Stage IIb, 73%; Stage IIIa, 56%; Stage IIIb, 38%; and Stage IV, 14%: M. Sutton

of Treatment for Advanced Cancer of the Cervix Uteri I. G. WILLIAMS and I. KAZEM. British Journal of Radiology [Brit. J. Radiol.] 35, 18-22, Jan., 1962. 2 figs.,

In this paper are presented the long-term results of treating 18 cases of advanced carcinoma of the cervix by 1-MeV. x rays alone at St. Bartholomew's Hospital. London. For technical reasons neither radium therapy nor surgery was feasible in these cases, and in all of them the disease was confined to the pelvis; 11 cases were Stage III, 6 were Stage IV, and one was Stage II. In 5 of the cases no biopsy examination was carried out.

The whole pelvic cavity was irradiated with 1-MeV. x rays (H.V.L. 9.3 mm: copper), a tumour dose of 6,000 r. in 6 weeks being given. Dysuria occurred in 5 cases and moderate diarrhoea in 8. In 2 cases treatment was terminated at a tumour dose of 4,500 r. owing to a severe moist reaction in the perineum. Four patients died in :the first year because of involvement of the ureters by the growth; 11 patients (61%) survived 3 years and 7-patients: (39%) lived for 5 years or more. One patient with an advanced, poorly differentiated, squamous carcinoma-of the cervical stump has survived 11 years.

Though the numbers are small, the authors regard the results as so encouraging as to justify an investigation > into the use of supervoltage radiotherapy alone in Stage; I and II carcinoma of the cervix uteria. M. Sutton,

1291. Treatment of Cancer of the Anus T. A. WATSON. Radiology [Radiology] 77, 783-787 Nov., 1961. 2 figs., 16 refs.

The author makes a plea for the use of interstitial radium in the treatment of cancer of the anus. He reports 9 cases, the whole experience of the Saskatoon Cancer Clinic, Saskatchewan, from 1947 to 1954. This represents only 4% of the 239 new cases of rectal cancer seen during the same period. Of the 9 cases seen, 6 were suitable for implantation. He states that the cases were all early ones [but no clinical or histological details are given]. The implants were made in 2 anteroposterior planes not more than 3 cm. apart and crossed at the lower ends only. The needles had an active length of 4.5 cm., the interior needles containing 1.5 mg. of radium and the outer needles twice as much. The dose at 0.5 cm. from the plane was 4,500 to 6,000 r. and the time usually 5 to 7 days. Three patients remain well 10 years later, one died after 2½ years with necrosis but no residual tumour, and one died-after 4 years from coronary disease with the anus completely healed. The sixth patient developed a recurrence after 84 years, and remains well after abdomino-perineal resection. Thus-5 out of 6 patients had a healed and normally functioning anus after radium treatment. It is claimed that these results are superior to those of external radiation and avoid the mutilation of radical surgery. Surgery, however, must be used for the inguinal nodes if enlarged, and growths extending upwards into the rectum are unsuitable for the interstitial method of treatment.

E. Stanley Lee

ABSTRACTS OF WORLD MEDICINE

Vol. 31 No. 6 June, 1962

Pathology

1292. The Production of Experimental Lung Cancer in Rats by Intratracheal Injection of 3:4-Вепгругене. (Опыт получения рака легких у крые путем интратражеального выедения 3,4-бензпирена)

V. A. RJAZANOV, K. A. BUŠTUEVA, and P. P. DVIŽKOV. Гивиена и Санитария [Gig. 1 Sanit.] 26, 3-6, Oct., 1961. 7 figs., 7 refs.

In these experiments, for which albino rats were chosen because primary lung carcinoma does not occur in these animals, benzpyrene was injected intratracheally as a solution in sunflower oil in two concentrations: control animals received oil only. In 8 control rats given one injection of 0.5 ml. of sunflower oil post-mortem examination showed only the typical changes of lipoid pneumonia. In the experimental animals one group of 4 rats received. one injection of 0.5 ml. of a 3:4-benzpyrene solution containing 1,000 µg. per ml. Necropsy 16 months later revealed no specific lung changes. A second group of 4 rats received one injection of 0.5 ml. of the benzpyrene solution containing 200 μ g. per ml. Some 15 months later one of these animals showed unmistakable signs of a primary lung carcinoma of the small round-cell type, while a similar tumour in an earlier stage of development was present in another. A final group of rats received 5 injections each of 0.5 ml. of the benzpyrene solution containing 200 μ g. per ml. One of these rats developed foci of round-cell infiltration with polymorphic cells and nuclei, indicating initial stages of malignant growth. Thus 3 of the 12 experimental rats developed typical changes of primary lung carcinoma following the intratracheal injection of 3:4-benzpyrene. Basil Haigh

1293. Lactate Dehydrogenase Activity in the Diagnosis of Mallenant Effusions

J. E. HORROCKS, J. KING, A. P. B. WAIND, and J. WARD. Journal of Clinical Pathology [J. clin. Path.] 15, 57-61, Jan., 1962. 15 refs.

A further investigation to assess the hypothesis that the ratio of lactate dehydrogenase (L.D.H.) activity in pleural or ascitic effusions to that in the serum is of value in the diagnosis of malignancy is reported in this paper from the North Lonsdale Hospital, Barrow in Furness Single results from each patient are reported in order that the results should not be weighted unfairly by serial estimations, which tend to give a constant average.

In 18 of 38 cases of malignant pleural effusion the serum L.D.H. level was above the normal value (70 to 230 i.u.) and in 25 the ratio of effusion enzyme activity to serum enzyme activity was "positive", that is, greater than unity; in 3 cases with a negative ratio the effusion was

shown to contain malignant cells. Of 24 cases of benign pleural effusion the serum enzyme level was raised in 7. and 16 presented a positive ratio. Similar inconsequential results were obtained in 10 cases of malignant ascites and in 5 of benign ascites. Estimations of malate dehydrogenase, glutamate-oxalacetate and glutamatepyruvate transaminase, and alkaline phosphatase activities were performed simultaneously for comparison. In general, positivity in benign effusions showed a closer relationship to the state of inflammation than to transudation. The authors consider that "clearly the problem is not one of glycolysis alone nor of malignancy per se" and conclude that " the assay of lactate dehydrogenase activity of effusions has no value in the diagnosis of malignancy". Harry Coke

1294. Serum γ -Glutamyl Transpeptidase Activity in Liver Disease

E. SZCZEKLIK, M. ORŁOWSKI, and A. SZEWCZUK. Gastroenterology [Gastroenterology] 41, 353-359, Oct., 1961. 3 figs., 6 refs.

At the Institute of Immunology, Wroclaw, Poland, the serum γ -glutamyl transpeptidase level was determined by a colorimetric method in the serum of 60 healthy subjects and of 72 patients with various types of liver disease and compared with the serum aldolase, phosphohexose isomerase, and alkaline phosphatase activity.

Only moderate increases in the transpeptidase activity were found in 20 cases of viral hepatitis and 13 of chronic hepatitis. Very high activity, however (sometimes as high as 100 times the normal value), was found among 21 cases of obstructive jaundice, 8 of biliary cirrhosis, and 10 of liver neoplasia. It is suggested that very high transpeptidase activity, not associated with jaundice, should be regarded as highly suggestive of metastatic cancer of the liver.

L. A. Elson

1295. A Rapid Method for the Determination of Urea in Blood and Urine

J. M. LEVINE, R. LEON, and F. STEIGMANN. *Clinical Chemistry* [Clin. Chem.] 7, 488–493, Oct. [received Dec.], 1961. 2 figs., 8 refs.

Although there are many compounds in body fluids which give a colour reaction with p-dimethylamino-benzaldehyde—Ehrlich's reagent—most are aromatic and can consequently be removed with activated charcoal. When urine or deproteinized blood is treated in this way the only chromogen remaining in the supernatant fluid after charcoal absorption is urea. This principle has been used as the basis for a simple assay

·2c

procedure for determining the concentration of urea in blood or urine. The authors, working at the Cook County Hospital, Chicago, claim that the test can be performed in 15 minutes and is accurate to 2 mg. of urea per 100 ml. of blood. [The large volume of blood necessary, 3 ml., might tend to limit the usefulness of the test in clinical practice.]

M. Sandler

HAEMATOLOGY -

1296. Comparison of the Thrombotest with the One-stage Prothrombin Time

A. J. QUICK and C. V. HUSSEY. New England Journal of Medicine [New Engl. J. Med.] 265, 1286-1289, Dec. 28, 1961. 18 refs.

It has been claimed that the thrombotest developed by Owren in Oslo (Lancet, 1959, 2, 754; Abstr. Wld Med., 1960, 27, 427) is more satisfactory for controlling anti-coagulant therapy than Quick's one-stage prothrombin time test, but in none of the comparative studies of the two tests on which such claims are based was the Quick test used as originally outlined by the present senior author, that is, with acetone-dehydrated rabbit brain as the thromboplastin, a reagent which has a high and constant potency. The results of a true comparative investigation are here reported from Marquette University School of Medicine, Milwaukee.

With the thrombotest the normal range was found to vary between 35 and 45 seconds, while the normal for the Quick test was 12 seconds. In 3 cases of classic haemophilia and 2 cases of severe haemophilia-B (Christmas disease, in which there is a pronounced deficiency of Factor IX) the thrombotest gave a prothrombin time within normal limits, but this was slightly prolonged in a patient with congenital thrombocytopenia; in all these. patients the Quick test result was 12 seconds. In 2 cases of congenital true hypoprothrombinaemia the results of the two tests correlated well. Both tests also gave a prolonged prothrombin time in a patient with severe Factor-VII deficiency, but only the Quick test showed a slight prolongation of prothrombin time in the patient's mother. In a few patients receiving bishydroxycoumarin the test results correlated well. It is noted that both tests are influenced by a decrease in Factor VII and also in prothrombin, neither is affected by a lack of Factor IX, but the thrombotest does not possess the sensitivity of the basic one-stage prothrombin test.

The authors also showed that if aged serum or Factor VII is added to the plasma it restores any Factor-VII deficiency and the Quick test becomes specific for prothrombin, while the addition of rabbit plasma absorbed with tribasic calcium phosphate restores the prothrombin time to normal in cases of congenital lack of Factor V. In a small series of ratients undergoing long-term anticoagulant therapy the addition of aged serum to the plasma shortened the prothrombin time. As long as the basic prothrombin time was below 20 seconds the corrected value tended to remain at 12 seconds, indicating that the amount of free prothrombin was not diminished. Above this level a fairly consistent ratio of the basic

prothrombin time to the serum corrected time was observed. It is pointed out that the primary effect of coumarin drugs is to depress Factor VII and this in turn brings about a lowering of the prothrombin level. If the basic prothrombin time is maintained at 25 seconds the danger of bleeding is rarely as serious as that of recurrent thrombo-embolism would be. A. Ackroyd

1297. ABO Groups and Rh Genotypes in the Elderly S. MURRAY. British Medical Journal [Brit. med. J.] 2, 1472–1474, Dec. 2, 1961. 10 refs.

If possession of a particular blood group confers disadvantages, then the distribution of that particular blood group among younger persons might be expected to differ from that found in older age groups. As the author found such difference among the paternal grandparents of infants with haemolytic disease of the newborn, she has now investigated, at the Regional [Blood] Transfusion Centre, Newcastle upon Tyne, the distribution of ABO blood groups and Rh genotypes among 633 elderly people ranging in age from 65 to 104 years. This series was subdivided into those who were ill, that is, patients in geriatric units, and those who were apparently well and active, and it was also divided by sex. Two statistically significant results were obtained: (1) an increased proportion of persons with blood of Group A in the healthy male group, and (2) an increase in the proportion of homozygotes D/D in the healthy group, particularly among the males. The author concludes her paper with the words "it is hoped that this series will help towards planning future work".

[Indeed, but much larger numbers are required to confirm these trends and future workers will be able to build on the foundations laid by the present author and might also include previous work on age, sex, and ABO groups which are unfortunately not referred to in this paper.]

I. Dunsford

1298. Determination of Human Platelet Survival Utilizing C^{14} -Labelled Serotonin

R. M. HEYSSEL. Journal of Clinical Investigation [J. clin. Invest.] 40, 2134–2142, Dec., 1961. 8 figs., 19 refs.

It is pointed out that tagging platelets with serotonin labelled with radioactive carbon (14C) has in theory certain advantages over other techniques of labelling, because serotonin is preferentially concentrated in platelets both in vivo and in vitro and the platelets need not be isolated to obtain labelling in vivo. At the Vanderbilt University School of Medicine, Nashville, Tennessee, platelet survival was studied in healthy subjects and in patients with thrombocytopenia, experiments being carried out with both autologous and homologous platelets.

The half-time of the ¹⁴C-labelled serotonin in circulating platelets was found to be 5 to 6 days, with less than 20% activity at 8 to 13 days. It is pointed out that these values are of the same order as those obtained by other labelling techniques—for example, with radioactive chromium and radioactive disopropylfluorophosphate. The loss of ¹⁴C-labelled serotonin indicated an experimental disappearance of platelets from the circulation.

It is stated, however, that the data are insufficient to settle the question of whether platelets normally are utilized (which would result in random destruction) or whether they age and die in the circulation. Comparison of the number of infusec labelled platelets in the circulation with the calculated number gave an average figure of 50 to 55% in the peripheral blood at the end of 24 hours, which is compatible with other estimates of a relatively small total platelet pool.

[This is an important paper which all interested in the measurement of platelet life-span should read.]

J. V. Dacie

1299. Lymphocyte Glycogen Content in Various Diseases R. V. Jones, G. P. Goffi, and M. S. R. Hutt. *Journal of Clinical Pathology [J. clin. Path.*] 15, 36–39, Jan., 1962. 1 fig., 5 refs.

An increase in the glycogen content of the lymphocytes in the peripheral blood has been reported in a number of diseases of the lymphoid system, these including chronic and subacute lymphatic leukaemia, lymphosarcoma, Hodgkin's disease, and some cases of infectious mono-The present study, reported from St. Thomas's Hospital Medical School, London, was extended to cover a number of diseases not primarily affecting the lymphoid system. The lymphocyte glycogen content was measured semi-quantitatively by the periodic-acid-Schiff (P.A.S.) technique in peripheral blood films from 31 control patients who showed no evidence of acute inflammation, chronic sepsis, carcinoma, or diseases of the reticulo-endothelial system, 30 patients with malignant epithelial tumours, 17 with lymphosarcoma, 13 with chronic lymphatic leukaemia. 22 with Hodgkin's disease, 9 with infectious mononucleosis, and 16 patients with miscellaneous disorders.

The results showed that an increased lymphocytic glycogen content may occur in disorders which do not primarily affect the lymphoid system, such as carcinoma and chronic suppuration. Although the lymphocytes of patients with chronic lymphatic leukaemia, lymphosarcoma, or Hodgkin's disease often showed a higher glycogen content than was found in other disorders, determination of the lymphocyte glycogen content is of little value as a diagnostic test. The findings of this study suggest that a high lymphocyte glycogen content is produced by several different mechanisms.

A. W. H. Foxell

1300. Control of Blood Haemoglobin Determinations by a Simple Effective Method

I. SCHOEN and M. SOLOMON. Journal of Clinical Pathology [J. clin. Path.] 15, 44-46, Jan., 1962. 3 refs.

From Mount Sinai Hospital, Los Angeles, a method is described for the preparation of a haemoglobin solution which may be used as a precision control of routine haemoglobin estimations. Both old, outdated, bloodbank citrated blood and pooled oxalated patient's blood give equally satisfactory results. The procedure used for haemoglobin estimation was the spectrophotometric cyanmethaemoglobin method. The control specimens may be prepared in either of the following ways: (1) outdated blood-bank blood is frozen in aliquots of 0.5 ml.

and kept at a temperature of -8 to -13° C.; each day a control aliquot is thawed and used. The specimen was found to be always well-haemolysed, dark red, and clear after thawing. (2) A pool of about "20 oxalated haematology blood specimens" is well mixed and 0.5-ml. aliquots withdrawn as described above. When thawed this blood is brighter red than the citrated blood.

It was noted that occasionally specimens from either series developed early brownish discoloration and turbidity during the test, but this disappeared during colour development and the reading was reproducible. If coagulum particles formed which interfered with pipetting the specimen was discarded. These control bloods maintained reliability and accuracy for periods of one to 2 years from a single batch of control material.

A. W. H. Foxell

MORBID ANATOMY AND CYTOLOGY

1301. Changes in the Portal and Splenic Veins in Portal Hypertension and Their Relation to Splenomegaly J. B. Wilson. *Gut* [*Gut*] 2, 310–315, Dec., 1961. 6 figs., 20 refs.

In this study, reported from the University of Edinburgh, of the changes in the portal venous system and the spleen in portal hypertension paraffin sections of the portal and splenic veins obtained from 31 cases of hepatic cirrhosis were examined; the portal veins from 2 healthy subjects were studied for comparison. In the cirrhotic patients the veins showed slight to marked muscle and elastic hypertrophy; these changes, also the co-existent splenomegaly, were directly related to the duration of portal hypertension. Intimal fibro-elastic thickening with or without small recent mural thrombi was commonly found, and in 3 cases there was a large mural thrombus in the portal vein.

A. Wynn Williams

1302. Electron-microscopic Findings in the Epithelial Cells of the Liver in Viral Hepatitis. (Elektronenmikroskopische Befunde an den Leberepithelzellen bei Virushepatitis)

L. COSSEL. Acta hepato-splenologica [Acta hepato-splenol. (Stuttg.)] 8, 333-356, Dec., 1961. 11 figs., 39 refs.

This paper from the Karl Marx University, Leipzig, is based mainly on the liver biopsy findings by electron microscopy on the first and second days of icterus in 2 patients with viral hepatitis. The techniques used in the preparation of the specimens for electron microscopy are briefly outlined and references are quoted. The findings by light microscopy are briefly described and it is suggested that the vacuolization of the endoplasmatic reticulum observed by electron microscopy may correspond to the clear liver cells seen by light microscopy; however, the author leaves this point undecided.

Non-specific findings are first described. These differed only in degree, extent, or frequency from those found in 46 normal control subjects. They can also be produced in animal experiments. In assessing them, due regard must be had to the differing functional activity of liver cells in different areas and at different times. In

hepatitis the liver cell nuclei are larger, there is more variation in cell size, bizarre forms are more common, and the nuclear membrane may show shell-like condensation. Nucleoli are more frequent than in normal subjects. The cytoplasm of the liver cells shows increased vacuolation due to the accentuation and dilatation of the endoplasmatic reticulum. Similar, though less marked, changes may be seen in experimental animals. They are usually associated with a decrease or loss of ribonucleoprotein granules and a decrease or even disappearance of the ergastoplasm. In hepatitis the ribonucleoprotein granules are always fewer in number than in normal cells and the Golgi fields are diminished. The mitochondria also differ quantitatively from those of normal cells, often being increased, indicating increased metabolic activity.

The specific findings consist in the presence of particles 200 to 2,400 Å in size, whose size and structure correspond to the electron microscopical picture of virus particles. They are round or oval, rarely irregular, and are sometimes composed of granules 90 to 110 Å in size. They may be compact or annular and often contain a central body of 90 to 630 A. They are situated in the cytoplasmatic ground substance or in vacuoles of the endoplasmatic reticulum. The smaller forms may show diffuse distribution through the liver cells. In liver cells containing virus particles ribonucleoprotein granules are diminished in number or absent. The affected liver cells show evidence of necrobiosis, band-like, homogeneous condensation of the plasma along the cell membrane, and a varying degree of dissolution of the cell membrane with loss of cytoplasm into Disse's space.

The significance of these particles and their possible relation to the ribonucleoprotein granules is discussed with reference to the findings of other workers.

[The paper is accompanied by excellent illustrations.]

F. Hillman

1303. A Quantitative Study of Coronary Arterial Calcification

L. E. BOLICK and D. H. BLANKENHORN. American Journal of Pathology [Amer. J. Path.] 39, 511-519, Nov., 1961. 5 figs., 7 refs.

Up to the present it has been difficult to study the structural pattern of calcification in arteries with advanced atheroma since the vessels must be decalcified before they can be properly sectioned. Working at the University of Southern California School of Medicine, Los Angeles, the authors have evolved a quantitative method for decalcifying tissue in which the calcium is extracted with 0.34 M ammonium ethylenediamine tetra-acetic acid at 5° C. for 14 days. The calcium content of the extracting medium is estimated at frequent intervals. The results indicated that atheromatous calcification of the coronary arteries can be as extensive as that which occurs in aortic atherosclerosis. There was evidence to suggest the occurrence of two different forms of calcification in coronary atheroma. Thus in some lesions which showed haematoxylin-ringed lacunae after decalcification the rate of removal of calcium was slow and it is suggested that in these cases calcium salts are present in discrete granules. Other coronary specimens could be more rapidly decalcified and these showed no lacunae; such lesions are believed to be more diffusely infiltrated by calcium.

G. Loewi

1304. The Natural History of Coronary Atherosclerosis J. P. Strong and H. C. McGill Jr. American Journal of Pathology [Amer. J. Path.] 40, 37-49, Jan., 1962. 2 figs., 19 refs.

The authors of this paper from the Louisiana State University School of Medicine, New Orleans, studied the natural history of coronary atherosclerosis in the coronary arteries obtained at necropsy on 548 patients aged 1 to 69 years. The arteries were opened lengthwise and the epicardial fat dissected off, the atherosclerotic lesions, when present, being then graded and examined. The authors discuss and tabulate the incidence of atherosclerotic lesions by age, race, and sex. A definite relationship was established between coronary artery disease and atherosclerotic lesions, and from their data the authors conclude that the presence of atherosclerosis rather than thrombosis determines the subsequent occurrence of ischaemic cardiac disease. The data also suggest that the basis of the atherosclerotic lesion is laid at least 20 years before any clinical effect becomes apparent. Possible aetiological factors responsible for these lesions should therefore be looked for at an earlier period of life. J. B. Wilson

1305. Metaplasia of the Bronchial Mucosa in the Absence of Carcinoma of the Bronchus. (Uber Metaplasien der Bronchialschleimhaut bei Fällen ohne Bronchialcarcinom)

C.-A. HACKETHAL and G. KÖNN. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie [Beitr. path. Anat.] 125, 445-456, Dec., 1961 [received Feb., 1962]. 8 figs., 21 refs.

The authors, writing from the Institute of Pathology, University of Freiburg im Breisgau, first review the literature on the subject of metaplasia of the bronchial mucosa. They then describe their own findings in the post-mortem examination of the lungs of 80 unselected subjects aged 15 months to 80 years, of whom 46 were over 50 and 48 were males. The lungs were examined under the dissecting microscope with 18 × magnification and suspicious areas were charted and sectioned, either serially or stepwise, and stained with haematoxylin and cosin and by van Gieson's method. A total of 560 sections were cut.

Established bronchial metaplasia was found in 11 cases and early metaplasia in 8. In 12 of the 80 cases the lungs showed chronic inflammatory changes and in 7 of them metaplasia was present. Of the remaining 68 cases, 12 showed metaplasia. Early metaplasia ("premetaplasia") was present in 3 of the cases without inflammation and consisted in an accumulation of small, dark cells, 3 to 5 layers deep, just above the basement membrane. The surface epithelium was ciliated and columnar. Laterally, these aggregates gradually thinned. The underlying tunica propria showed isolated round-cell infiltrates. In 5 specimens with chronic inflammatory changes and in 7 without, pre-metaplasia consisted

in aggregates of larger, round to oval cells, with an open nucleus and a broad rim of cytoplasm. They were 2 to 4 layers deep. The surface epithelium was normal. Occasionally these foci showed mitoses. Laterally they faded very gradually. The basal membrane was oedematous and widened. The tunica propria contained acute and chronic inflammatory cells. In 2 cases with chronic inflammation and 6 without, the lungs showed transitional metaplasia, 4 to 6 cells deep. The nuclei were large and loosely arranged and the cytoplasm distinct, and occasional mitoses were seen. The ciliated surface was replaced by somewhat flattened round cells. The basal membrane was thickened, sometimes strikingly so, and the tunica propria showed chronic inflammatory infiltrates and scars. Two cases with chronic inflammatory disease showed squamous metaplasia, extending in one of them into the ducts of mucous glands. In most cases the appearance under the dissecting microscope of whitish or grey ill-defined foci, sometimes with slight elevation, corresponded to the areas of metaplasia. Occasionally these foci were due to large mucous glands or cartilage.

Thus metaplasia was found in 24% of the cases examined. This figure is compared with those from several series reported in the literature, ranging from 7% to 44%. It would appear that the incidence of metaplasia is related to chronic infection, but not to neoplasia.

F. Hillman

1306. The Concept of Organizing Pneumonia P. Gross and E. J. Benz. Archives of Pathology [Arch. Path.] 72, 607-619, Dec., 1961. 16 figs., 8 refs.

The histopathological changes in the lungs in 29 cases in which "organizing pneumonia" had been diagnosed were studied at St. Luke's Hospital, Bethlehem, Pennsylvania. The definitive criterion for this diagnosis was the demonstration of reticulin fibres within what had been interpreted as intra-alveolar exudate.

The outstanding feature in each case was that the alveolar walls were generally moderately to severely thickened by non-collagenous reticulin tissue, frequently rich in ovoid fibroblast-like or round lymphocyte-like nuclei. The reticulin framework of the thickened alveoli frequently showed evidence of degeneration as indicated by foci of condensation, fragmentation, and lysis of fibres. In some cases the reticulin fibres extended from the alveolar walls into air spaces so as to fill them except for a peripheral cleft. The similarity of the appearance of the reticulin in the intra-alveolar tissue (coarseness of fibres and intricacy of the branching) to the reticulin in the alveolar wall suggested that the former was laid down at about the same time that the alveolar walls became thickened. Even in cases with marked intra-alveolar leucocyte and fibroblast-like exudate the reticulin fibres showed evidence of degeneration (fragmentation, condensation, lysis) rather than of new fibre. formation.

In the authors' view the intra-alveolar stroma is old and degenerating. Furthermore, in every case thickening of the septal walls by an accretive proliferative process was demonstrated. Thus they conclude that all the patients suffered from an accretive chronic interstitial pneumonitis in which there was a potential re-establishment of air spaces by a degenerative and necrotizing process affecting primarily the occluding intra-alveolar tissue. The corollary to this conclusion is that there is no organization in these cases of "organizing" pneumonia.

H. Caplan

1307. Histological Changes in the Thyroid in Cirrhosis of the Liver

A. NICOL and G. SCLARE. Journal of Clinical Pathology [J. clin. Path.] 15, 26-30, Jan., 1962. 1 fig., 34 refs.

The association between cirrhosis of the liver and chronic thyroiditis has been reported on many occasions. Recent work has suggested that this association may be the result of autoimmunization affecting both organs more or less simultaneously. In the present study the authors assessed histologically the condition of the thyroid gland in 77 cases of cirrhosis of the liver in 43 men aged 19 to 85 (mean 50·8) years and 34 women aged 27 to 74 (mean 57·4) years who came to necropsy at Manchester Royal Infirmary during the period 1954–60. In 54 cases the cirrhosis was classified as portal, in 14 as biliary, and in 9 as cardiac. An equal number of nonhepatic cases were examined post mortem as a control.

No difference was found between the incidence or severity of lymphocytic infiltration of the thyroid gland in the cirrhotic and control groups. There was, however, a significant fibrosis or "cirrhosis" of the gland, unrelated to lymphocytic infiltration, associated with cirrhosis of the liver, especially in women aged 50 years and over. The authors review the literature of the subject, and discuss possible theories to account for this association between thyroiditis and liver disease. They conclude that, although there is no definite evidence in favour of any one theory, the occurrence of "cirrhosis of the thyroid" in association with several different types of liver damage of varying aetiology points to disordered liver function as being the principal factor in the pathogenesis of the thyroid lesion. A. W. H. Foxell

1308. The Inflammatory Process in Rheumatic Fever. (Le processus inflammatoire de la maladie de Bouillaud) R. LUTEMBACHER. Archives des maladies du cœur et des valsseaux [Arch. Mal. Cœur] 54, 1177-1184, Nov., 1961 [received Jan., 1962]. 2 figs.

This paper sets out, with numerous references to the literature, the general thoughts of the author on various manifestations of rheumatic fever. In children, he states, myocarditis plays the main role, whereas valvulitis is exceptional and does not lead to permanent lesions, the murmurs which are heard being a sign of myocarditis. The presence of Aschoff bodies and fibrinoid necrosis are the hallmarks of the underlying inflammatory process. In the adult, although the clinical manifestations are different, the same histological signs are found. Late recrudescences of rheumatic fever do not affect the condition of a diseased sclerosed valve, although murmurs may be modified by myocarditis or spread of the disease to another valve. The differences in behaviour of the rheumatic process in the child and in the adult are explained on the basis of supposed differences in the permeability of the ground substance. G. Loewi

Microbiology and Parasitology

1309. Viruses Isolated from Natural Common Colds in the U.S.A.

D. HAMRE and J. J. PROCKNOW. British Medical Journal [Brit. med. J.] 2, 1382-1385, Nov. 25, 1961. 17 refs.

Earlier work by British virologists demonstrating the part played by a new group of viruses, the rhinoviruses, in the causation of a proportion of common colds receives confirmation in an investigation of the viral actiology of natural common colds over an 8-month period in 103 preclinical medical students. The volunteers reported to the laboratory at the first sign of a cold, and nose and throat swabs were collected in duplicate, one set being for virological, the other for bacteriological examination. The swabs for virus isolation were placed in phosphate-buffered saline containing 0.5% bovine albumin, inoculation being carried out the same day into secondary tissue cultures of human embryo kidney and monkey kidney and into cultures of the continuous line of human malignant cells, H-Ep 2. The human and monkey kidney cultures were incubated at 33° C. on a roller drum and maintained in a medium containing 0.03% of sodium bicarbonate. The H-Ep 2 cultures were incubated stationary at 36° C. Cultures were observed for cytopathic effect and the monkey kidney cultures tested for the presence of haemabsorbing viruses.

From 199 specimens obtained early in the course of a cold, 53 viruses were isolated, in contrast to the isolation of two viruses from 456 specimens collected at routine visits when the volunteers were symptom-free. The viruses from the cases of colds comprised 24 strains which would only grow in human kidney, 7 capable of growing in both human and monkey kidney, 8 strains of E.C.H.O. 28, 11 strains of respiratory syncytial virus, and 3 strains of para-influenza virus. Although the 7 strains capable of growing in human and monkey kidney resembled the Salisbury strain H.G.P., they were not neutralized by an anti-H.G.P. serum. The 2 strains from the asymptomatic individuals grew only in human kidney and were isolated at periods when colds were prevalent. The authors point out that they identified the causative agent in 28% of the colds and that serological methods employing the new viruses may help to increase this percentage in future studies. J. E. M. Whitehead

1310. Attempt to Interpret Certain Failures of the Complement Fixation Reaction in Poliomyelitis by Means of the Complement Fixation Inhibition Reaction. (Essai d'interprétation de certaines défaillances de la réaction de fixation du complément dans la poliomyélite au moyen de la réaction d'inhibition de la fixation du complément)

C. CHASTEL and J. VIRAT. Annales de l'Institut Pasteur [Ann. Inst. Pasteur] 101, 505-522, Oct., 1961. 8 refs.

In the course of the 2 years 1959 and 1960 tests carried out at the Institut Pasteur, Paris, on sera from several hundred patients from whom poliovirus had been

isolated showed that 17% gave a negative complement fixation reaction. Of these sera 32 were then examined by an indirect test for inhibition of complement fixation; in this the serum was incubated with poliomyelitis virus at 37° C. for 45 minutes, a standard positive serum was then added, and the mixture left overnight at 4° C. before the haemolytic system was added. It was shown that 8 sera from patients with Type-1 poliovirus and 2 sera from those with Type-2 virus caused inhibition. Antibody inhibiting complement fixation with Type-1 virus was specific, but one of the sera inhibiting Type-2 virus also inhibited Type 1, though to a lower titre. Serum from 5 cases of Type-1 and 3 cases of Type-3 poliomyelitis gave negative results in inhibition tests, but were found to fix complement with I unit of antigen. The 14 remaining sera were negative by both tests, as were 18 sera from patients with other illnesses.

As inhibiting antibody was shown to be present in sera obtained during the acute phase of the illness but was absent during convalescence, it is concluded that such antibody appears early, before the results of isolation tests are known, and that its presence is transient. It is considered that the test is too complicated to be used for early diagnosis, but may be useful in research studies and in potency tests on vaccines.

Janice Taverne

1311. Evaluation of the Kveim Reaction as a Diagnostic Test for Sarcoidosis

J. G. Hirsch, Z. A. Cohn, S. I. Morse, R. W. Schaedler, L. E. Siltzbach, J. T. Ellis, and M. W. Chase. New England Journal of Medicine [New Engl. J. Med.] 265, 827–830, Oct. 26, 1961. 3 figs., 15 refs.

An investigation designed objectively to assess the value of the Kveim reaction in the diagnosis of sarcoidosis was carried out at the Rockefeller Institute Hospital, New York. Kveim antigen was prepared by a new method from spleen heavily infiltrated with sarcoid nodules to give a suspension in buffered saline containing up to 6 mg. of total solids per ml. [For full details of this new technique the original paper should be consulted.] Patients received an intradermal injection of 0.15 ml: of Kveim suspension and 4 to 6 weeks afterwards the inoculation sites were examined and removed by punch biopsy. Several sections were prepared and stained with haematoxylin and eosin. The biopsy specimens were evaluated independently by two observers who were unaware of the clinical features of the case. All specimens were examined under polarized light to permit detection of birefringent foreign materials. The main histological criterion of a positive result of the Kveim test was the presence of well-organized aggregates of epithelioid cells, with or without giant cells.

A positive result was obtained in approximately 75% of patients with subacute sarcoidosis, 64% of those with chronic sarcoidosis, and in less than 5% of the patients with other diseases.

D. Geraint James

Pharmacology and Therapeutics

1312. Clinical Evaluation of Phendimetrazine Bitartrate C. Ressler and S. H. Schneider. Clinical Pharmacology and Therapeutics [Clin. Pharmacol. Ther.] 2, 727-732, Nov.-Dec., 1961. 3 figs., 6 refs.

Clinical investigation of a phenmetrazine congener, phendimetrazine, was performed by using double blind controls. Of 50 obese patients who participated, 36 completed one adequate course of active drug or placebo and 20 completed both phases of the study. The average total weight lost and the average weight lost weekly by patients who received phendimetrazine were about 20 times as much as those of patients who received placebo. Comparison of the two groups showed no significant difference in undesirable effects. The over-all incidence of subjective complaints or minor toxic reactions was negligible, and examination including pulse, blood pressure, blood count, and urinalysis showed no evidence of major change.—[Authors' summary.]

1313. Comparative Study with a New Antacid Tablet A. J. KAUVAR. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 671-677, Dec., 1961. 1 ref.

A double-blind comparative trial of a new antacid preparation ("neo-gel") in patients with radiologically proven duodenal ulcer is reported from General Rose Memorial Hospital, Denver, Colorado. Each tablet of the preparation contained 1.3 g. of colloidal tricalcium phosphate and 0.6 g. of magnesium trisilicate and its efficacy was compared with that of an inert tablet and that of "gelusil". [The author fails to state the composition of the last-named preparation, which contains in each tablet 0.25 g. of aluminium hydroxide gel and 0.5 g. of magnesium trisilicate, and to note that both active preparations contained magnesium trisilicate, but in unequal amounts.]. The three varieties of tablet were identical in appearance and each was administered to a group of 25 patients, the selection of treatment being randomized and the identity of the tablets unknown to the patients and physician. The dosage was two tablets every 2 hours while the patient was awake, continued for a minimum of 6 weeks in most cases. The patients were also given suitable diets, and most received phenobarbitone in a dosage of $\frac{1}{2}$ to $\frac{1}{2}$ gr. (16 to 32 mg.) 4 times daily; anticholinergic drugs were not administered. The series included both in-patients and out-patients [but the numbers of each are not stated]. The effect of treatment was evaluated weekly in each patient, and serial radiographs were obtained fortnightly until no changes in the radiological appearances were observed.

The therapeutic response was considered to be good in 22 of the 25 patients receiving neo-gel, in 16 out of 25 receiving gelusil, and in 10 of the 25 given the placebo. Gastric analysis before treatment showed a high free acidity in all patients; one week after the start of treatment the free acid fell to zero in all except one patient

given neo-gel, in all except 3 given gelusil, but in only 3 of the 25 patients given the placebo. The value of antacids in the treatment of duodenal ulcer has been confirmed by the findings of this investigation. [It cannot be concluded and the author does not claim, that the antacid combination tried is superior to existing antacids.]

J. J. Segall

1314. Symptomatic Treatment of Diarrhea with Diphenoxylate

A. WINKELSTEIN. American Journal of Gastroenterology [Amer. J. Gastroent.] 36, 692-697, Dec., 1961. 5 refs.

An evaluation of a new synthetic compound, diphenoxylate (2:2-diphenyl-4-(4-carbethoxy-4-phenyl-1-piperidino)butyronitrile hydrochloride), in the symptomatic treatment of acute and chronic diarrhoea is reported. The drug was given to 32 unselected patients (18 female and 14 male, aged 25 to 68 years) with diarrhoea, in whom the causative conditions were: functional diarrhoea (8 patients), acute gastro-enteritis (3), gastrogenous diarrhoea (5), antibiotic colitis (2), ulcerative colitis (7), regional ileitis (4), regional ileocolitis (1), and ileotransverse colostomy (2). The diarrhoea had been present for 1 to 4 weeks in 9 patients, 6 weeks to one year in 11 patients, 2 to 5 years in 7, and over 5 years in 5. Except in 2 cases, the drug was given in a dosage of 5 mg. 3 times daily initially (usually for about 3 weeks) followed by a maintenance dosage of 2.5 mg. three times a day; these were considered to be the optimum dosage levels. In all cases diphenoxylate effectively inhibited the passage of frequent and loose or watery stools and lessened the urge to defaecate; most of the patients passed one or two formed stools daily. The only side-effect observed was euphoria in 2 patients, the treatment being consequently discontinued. The drug did not have any excess constinuing effect.

The author considers that in the control of diarrhoea diphenoxylate is approximately as effective as codeine which has the disadvantage of frequently causing nausea; moreover, there has been no evidence of addiction to diphenoxylate. The drug apparently acts directly on the intestinal smooth muscle; there are no known contraindications.

J. J. Segall

1315. Acute Effects of Intravenous Chlorothiazide upon Cardiovascular Hemodynamics

M. A. Greene, A. J. Boltax, and E. S. Scherr. American Heart Journal [Amer. Heart J.] 62, 659-669, Nov., 1961. 20 refs.

This study was carried out at the Bronx Hospital, New York, in order to gain more information about the mechanism of action of chlorothiazide in reducing blood pressure, since this has never been properly established. The various possibilities proposed are briefly enumerated. The effect of the drug, which is limited to the hypertensive

state, was therefore studied in 12 patients, 5 women and 7 men, in 9 of whom the blood pressure was greater than 140/90 mm. Hg, one had an average control pressure of 187/75 mm. Hg, and 2 were normotensive. After a preliminary control period during which no hypotensive or diuretic drugs were given the acute effects of the intravenous injection of 0.75 to 1 g. of chlorothiazide were studied, numerous observations being made on the subjects both before and up to 170 minutes after administration of the drug. The right heart was catheterized in 10 cases.

In 7 of the hypertensive subjects there was a significant fall in the systolic, diastolic, and mean blood pressures by an average of 34%. There was also a significant fall in cardiac output in 4 of these subjects, which was associated with a reduction in stroke volume and central blood volume. The total peripheral resistance declined in 3 cases and increased in 3, but plasma and blood volumes did not change in those patients in whom they were measured. There was no consistent relationship between fluid balance and changes in cardiac dynamics. In the remaining 5 patients no significant change in blood pressure occurred. It is concluded that the findings of this immediate study (which may not necessarily apply to long-term treatment with the drug) suggest that the mechanisms of the antihypertensive action of chlorothiazide include vasodilatation. The vascular effects of the drug appear to depend on the existence of the hypertensive state, but the exact nature of these effects is still unknown G. Clayton

1316. Digitalis and the Pulmonary Circulation YUNG SUP KIM and D. M. AVIADO. American Heart Journal [Amer. Heart J.] 62, 680–686, Nov., 1961. 6 figs., 11 refs.

Much is known about the effects of digitalis on the heart, but its effects on the pulmonary circulation are still uncertain. They may best be defined by a systemic comparison of the following factors in human subjects and in dogs: (1) pulmonary arterial pressure; (2) pulmonary venous pressure; (3) pulmonary blood flow; and (4) the derived pulmonary vascular resistance; only the pulmonary arterial pressure can be measured directly in man. In such a study, carried out at the University of Pennsylvania, Philadelphia, dogs were anaesthetized with morphine and chloralose, respiration was maintained by means of a pump, and the left chest was opened to allow the introduction of catheters into the vessels of the left upper pulmonary lobe. In 8 dogs the mean pulmonary venous outflow was measured by collecting, measuring, and returning the effluent blood from the vein of the left lower lobe. In the other 14 dogs, in which the inflow perfusion of the left lower lobe was studied, the artery supplying this lobe was cannulated and supplied with blood from the right atrium through a "Sigmamotor" pump, the inflow pressure being recorded on a manometer and the flow by means of a rotameter. The three preparations of digitalis studied, namely, acetyl strophanthidin, digoxin, and ouabain, were injected into the femoral vein or the perfused pulmonary artery. In some cases the lungs were denervated by vagotomy and excision of the upper four thoracic sympathetic

ganglia, while atropine sulphate and bretylium tosylate were used to achieve selective blockade.

Within 2 minutes of the intravenous injection of acetyl strophanthidin there was a slight but consistent fall inboth systemic and pulmonary arterial pressures. The systemic pressure returned to normal in a few minutes, but the pulmonary pressure remained low. A small fall of 0.5 to 2 mm. Hg in the left atrial pressure may have contributed to this occurrence, but is not considered the exclusive cause. The pulmonary venous flow was reduced by a mean of 40%, a reduction which was not affected by vagotomy. By dividing pulmonary arterial pressure by venous flow the value for pulmonary vascular resistance was derived. In 5 of the dogs this factor showed a mean increase of 46%, and this occurred even after vagotomy and blockade with bretylium tosylate. In a series of 14 perfusion experiments a rise in pressure in the left lower lobar artery could be demonstrated following the injection of strophanthidin directly into that artery. This did not occur when alcohol (used as the solvent) alone was injected. There was little significant change in left atrial pressure. Vagotomy, sympathectomy, or intravenous injection of bretylium had little effect on this rise in pressure. A higher perfusion rate resulted in a higher arterial pressure, which became higher still following administration of strophanthidin. An increase in pulmonary vascular resistance was also observed following a fall in the pulmonary blood flow brought about by bleeding.

In a discussion of these results it is suggested that the rise in vascular resistance produced by strophanthidin would appear to be due to both a passive response to reduction in blood flow and also to the direct action of the drug on the pulmonary vessels. The exact location of this constriction has not been determined, but certainly the junction between the pulmonary veins and the left atrium can be excluded, as was shown by simultaneous measurement of pressures at these two sites. While these results are found in dogs, the situation in regard to the human lung is quite uncertain. The majority of patients show a reduction in calculated pulmonary vascular resistance on digitalization. However, many of these patients are suffering from heart disease and moreover various other factors are involved. G. Clayton

1317. The Effects of Angiotensin on Pulmonary Circulation and Ventricular Function

P. N. Yu, M. N. Luria, J. K. Finlayson, C. A. Stanfield, H. Constantine, and F. J. Flatley. *Circulation [Circulation]* 24, 1326–1337, Dec., 1961. 7 figs., 20 refs.

This paper from the University of Rochester School of Medicine and Dentistry, New York, describes studies on the cardiovascular effects of intravenous infusions of synthetic angiotensin octapeptide in patients and in dogs. Right heart catheterization was employed and, in the human studies, cardiac output was measured both by the Fick principle and by indicator dilution curves. The subjects were 16 normotensive patients without evidence of valvular disease. After baseline measurements had been made, angiotensin was infused continuously at a rate of 0.015 to 1.135 μ g, per kg, body weight per

minute, depending on the increase in systemic blood 1320. A Clinical Trial of Procaine Hydrochloride pressure; the optimum rate was found to be 0.05 to J. Hirsh. British Medical Journal [Brit. med. J.] 2 $0.10 \mu g$. per kg. per minute. Eight dogs were studied, the dose in these being 1 μ g. per kg. per minute.

The results were similar in both species studied. During angiotensin infusion there was a significant increase in systemic arterial pressure which began within 2 minutes of the start of the injection, could be satisfactorily maintained for an hour or more, and ceased within 2 or 3 minutes of stopping the infusion. There was an increase in pulmonary wedge pressure, assumed to reflect a rise in left ventricular end-diastolic pressure; the pulmonary. arterial pressure also rosé, but this was thought to be a secondary phenomenon rather than one due to active pulmonary vasoconstriction, since there was little change in the pressure gradient between the pulmonary artery and the left atrium. The cardiac output tended to fall during the infusion of angiotensin, though this change was slight and not statistically significant. There was a significant increase in the calculated total systemic and pulmonary vascular resistance, and also in the stroke work of both left and right ventricles. The upstroke time in the femoral arterial pulse tracing was prolonged and an anacrotic notch appeared in some cases. Studies of ventricular function curves in the dog indicated that these were altered during angiotensin infusion so that both ventricles performed more work at any given filling pressure.

The authors conclude that angiotensin is a very powerful pressor agent which acts mainly on the systemic circulation and that in the compensated human and canine heart it also has the effect of increasing myocardial contractility. M. Harington

1318. Trial of Procaine in the Aged

S. R. FEE and A. N. G. CLARK. British Medical Journal [Brit. med. J.] 2, 1680-1682, Dec. 23, 1961. 7 refs.

A clinical trial of procaine injections in 44 elderly patients over the period of one year is reported. Withone exception, no demonstrable effect was noted in a series of 24 bedfast and incontinent demented patients. A controlled trial with 40 elderly infirm residents in an old people's home showed no statistical difference between the effects of procaine and of saline injections.

It is concluded that procaine injections are of no value in these two groups of patients.—[Authors' summary.]

1319. Trial of Procaine in Old Age and Chronic Degenerative Disorders

J. A. W. BÉRRYMAN, H. A. W. FORBES, and R. SIMPSON-WHITE. British Medical Journal [Brit. med. J.] 2, 1683-1684, Dec. 23, 1961. 2 refs.

Twenty women patients aged over 50, suffering from various disorders, mostly of a degenerative nature, received procaine hydrochloride for one year, according to Aslan's technique. There was no evidence from this double-blind trial that these patients benefited from this therapy. There was no significant difference between the trend of this group and that of a control group of 20 similar patients.—[Authors' summary.]

1684-1685, Dec. 23, 1961. 7 refs.

A double-blind trial of procaine hydrochloride has shown no detectable change in the treated group as compared with a control group. It is concluded that its use as a rejuvenating agent is unjustified.—[Author's sum-

1321. Metabolic Effects of Paramethasone Acetate G. W. IRWIN, F. H. PRIEBE, and A. S. RIDOLFO. Metabolism: Clinical and Experimental [Metabolism] 10, 852-858, Nov., 1961. 5 figs., 2 refs.

Studies in animals had indicated that paramethasone acetate (6\alpha-fluoro-16\alpha-methyl prednisolone acetate) had a potent anti-inflammatory effect and a favourable electrolyte response. In this paper from Indiana University School of Medicine, Indianapolls, the authors describe the short-term effects of this steroid in 7 patients during 8 metabolic studies. The dosage of the drug ranged from 6 mg. to 15 mg. daily.

In none of the patients was there any change in the serum sodium or serum potassium concentrations, although there was a slight increase in the urinary excretion of sodium and potassium in some patients receiving the higher dosage. Likewise there was a minimal increase in urinary excretion of calcium and phosphorus. In one patient with active rheumatoid disease, previously in negative nitrogen balance, a decrease in urinary excretion of nitrogen and restoration of a positive nitrogen balance occurred; in the other studies, however, there was a slight increase in the urinary excretion of nitrogen. The haematological effects of paramethasone acetate were similar to those of other corticosteroids. At a dosage of 6 mg, daily there was depression of the urinary excretion of both 17-ketosteroids and 17-hydroxycorticoids. A. Gordon Beckett

The Renal Effects of Chlorothiazide

A. R. LAVENDER and T. N. PULLMAN. Journal of Pharmacology and Experimental Therapeutics [J. Pharmacol. exp. Ther.] 134, 281-285, Dec., 1961. 1 fig., 12 refs.

An investigation "to determine whether chlorothiazide acts directly on the kidney or indirectly through some secondary humoral or haemodynamic mechanism" is reported from the University of Chicago. Chlorothiazide was infused into one renal artery in each of 13. dogs in a concentration of 0.06 to 6.8 mg. per ml. at a rate of 1 ml. per minute, the other kidney serving as a control. The ureters were separately cannulated and urine was collected from the two kidneys in successive periods of 15 to 20 minutes. In all the dogs there was an increased excretion of chloride, sodium, and water, with a smaller increase in potassium excretion. Except in 2 dogs in which the response was limited to the infused kidney, the increase in excretion was bilateral, but greater in the infused than the control kidney. It is suggested that chlorothiazide acts directly at an intrarenal site, and, since there was no change in renal blood flow or glomerular filtration rate, this site "must be tubular in origin". V. J. Woolley

1323. The Effect of Dosage Regimen on the Diuretic Efficacy of Chlorothiazide in Human Subjects

J. MURPHY, W. CASEY, and L. LASAGNA. Journal of Pharmacology and Experimental Therapeutics [J. Pharmacol. exp. Ther.] 134, 286–290, Dec., 1961. 2 figs., 10 refs.

An attempt was made at Johns Hopkins University School of Medicine, Baltimore, Maryland, to determine whether or not the diuretic efficacy of chlorothiazide depended on the dosage regimen—that is, the spacing of doses. Ten healthy male subjects each received 5 treatmen'ts in random order: (1) chlorothiazide, 2 g. in a single dose at 8 a.m.; (2) chlorothiazide, 1 g. twice daily; (3) chlorothiazide, 0.5 g. 4 times daily; (4) chlorothiazide, 0.25 g. 8 times daily; and (5) a placebo. Each subject received the same number of tablets 8 times a day, so that, depending on the dosage schedule, the individual dose at any given time consisted wholly of chlorothiazide or placebo tablets or of both together. Collection and measurement of urine were made for the first 8 hours, the next 7 hours, and the last 9 hours of each experimental period; aliquots were also retained for electrolyte determination. In all cases a greater diuresis and electrolyte excretion occurred when the amount of chlorothiazide prescribed was divided into small doses given intermittently than when it was given as a single dose. The effect of giving probenecid in addition to the chlorothiazide was also studied, but the results were variable. V. J. Woolley

1324. Studies on the Respiratory, Circulatory and Analgesic Effects of 1(p-chlorophenethyl)-6:7-dimethoxy-2-methyl-1:2:3:4-tetrahydrolsoquinoline (Ro 4-1778/1) F. F. FOLDES, J. MOORE, and I. M. SUNA. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 682-693, Dec., 1961. 3 figs., 13 refs.

In this investigation, carried out at the Mercy Hospital, Pittsburgh, three groups of patients were premedicated intramuscularly with 100 mg. of pentobarbitone and 0.4 mg. of scopolamine, the 20 in Group 1 receiving in addition 100 mg. of pethidine. Anaesthesia was then induced with a sleep dose of thiopentone, an oral airway was inserted, and nitrous oxide and oxygen were administered from a circle absorption system. Patients in Groups 1 and 2 were given (at "zero time") 1 mg. of Ro 4-1778/1 per kg. body weight, the 12 in Group 2 also receiving 0.02 mg. of levallorphan per kg. 7 minutes after the Ro 4-1778/1. The 4 patients in Group 3 were given the same dose of levallorphan at "zero time", followed 5 minutes later by 1 mg. of Ro 4-1778/1 per kg. Respiratory and circulatory changes were measured before and at intervals after the injections. It was found that the initial dose of Ro 4-1778/1 produced considerable respiratory depression, and that this was more marked in the patients in Group 2, showing that the subsequent administration of levallorphan did not antagonize the depression. In the 4 patients given levallorphan first (that is, Group 3) this drug caused respiratory depression which was increased by the Ro 4-1778/1 injected 5 minutes later. Ro 4-1778/1, alone or with levallorphan, produced only moderate changes in pulse rate and blood pressure.

To the 20 patients in Group 1 further doses of Ro 4-1778/1 and thiopentone were given throughout surgery and the results compared with those in a similar series of patients given pethidine as the anaesthetic adjuvant. It was found that the duration of action of Ro 4-1778/1 was more prolonged than that of pethidine and that the degree of analgesia produced by 1 mg. of Ro 4-1778/1 per kg. was about the same as that obtained with 0.5 mg. of pethidine per kg.

Mark Swerdlow

1325. Double-blind Evaluation of a New Analgesic Agent in Postextraction Pain

N. W. CHILTON, A. LEWANDOWSKI, and J. R. CAMERON. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 702-706, Dec., 1961. 7 refs.

A preliminary pilot study carried out at Temple University School of Dentistry, Philadelphia, suggested that 60 mg, of Ro 4-1778/1 taken every 4 hours by mouth provided effective analgesia and was free from side-effects. The authors then carried out a double-blind study in which the effects of Ro 4-1778/1 (60 mg.), codeine (60 mg.), dextropropoxyphene (65 mg.), and a placebo, administered in random order, were compared in 600 patients attending for dental extractions, the subjects being asked to take one capsule 4-hourly postoperatively and to return 48 hours later with the unused portion of the medication. In the event 14% of the patients did not require an analgesic. Codeine proved more effective than dextropropoxyphene or the placebo and equally as effective as Ro 4-1778/1. However, the placebo produced adequate pain relief in 87.7% of the patients who took it. There were fewer side-effects with Ro 4-1778/1 and dextropropoxyphene than with codeine.

Mark Swerdlow

1326. Two New Butyrophenone Derivatives Studied with the Conditioned Reflex Technique

G. F. GOLWURM and F. VANNI. Diseases of the Nervous. System [Dis. nerv. Syst.] 22, 623-627, Nov., 1961. 4 figs., 10 refs.

In this study the authors present results of experiments designed to evaluate the effect of two new members of the butyrophenone group of drugs: (1) R-1625 [4'fluoro-4-(4'-4''-chlorophenyi)-4'-hydroxypiperidine-butyrophenone], and (2) R-1647 [4'-methoxyl-4-1-(4'-phenyl)-1:2:3:4-tetrahydropyridine-butyrophenone]. They observed the effect of subcutaneous administration of the drugs in varying dosages on the well-stabilized conditioned responses of avoiding weak electric shocks in rats.

As regards R-1625, while its ability to inhibit the conditioned reflex was high (like that of chlorpromazine and reserpine), it showed no activity in conflict situations, as expressed by the "emotional tensions" in these rats. The latter was marked with R-1647, but was below that seen with anti-anxiety compounds such as benactyzine and meprobamate.

The authors postulate that as the activity of R-1625 is similar to that of the phenothiazines and reserpine, this compound may be similarly useful for the same psychotic symptoms.

N. Rathod

Chemotherapy

1327. Sulfamoxole ("Nuprin"), a New Sulfonamide, in Pediatric Practice

J. A. Dugger. Journal of New Drugs [J. New Drugs] 1, 223-229, Sept.-Oct., 1961 [received Feb., 1962]. 2 figs., 6 refs.

In this paper from Borgess Hospital Research Department, Kalamazoo, Michigan, a trial is reported of a new sulphonamide, sulphamoxole, in 151 patients, including 131 whose ages ranged from 6 months to 10 years. Nearly all the conditions treated were infections of the ear, nose, and throat and respiratory tract. In infants the dosage was 25 mg. per kg. body weight twice daily for the first day or two followed by half this dosage for the duration of treatment. Older children received 1 g. twice on the first day and 0.5 g. twice daily thereafter. The results were considered to be good in 77% and fair in 12.3%. Treatment had to be discontinued in 3 cases only, because of drug rash in 2 and crysalluria in one; these side-effects disappeared when treatment ceased.

V. J. Woollev

1328. Severe Reactions to Long-acting Sulfonamides. Erythema Multiforme Exudativum and Lupus Erythematosus following Administration of Sulfamethoxypyridazine and Sulfadimethoxine

M, L. RALLISON, J. O'BRIEN, and R. A. GOOD. Pediatrics [Pediatrics] 28, 908-917, Dec., 1961. 6 figs., 42 refs.

The authors of this paper from the University of Minnesota Medical School, Minneapolis, report the occurrence of erythema multiforme exudativum (in 2 patients) and lupus erythematosus (in one patient) following administration of the long-acting sulphonamides sulphamethoxypyridazine and sulphadimethoxine. Erythema multiforme exudativum developed in a girl aged 34 years 10 days after starting a course of sulphamethoxypyridazine in a dosage of 250 mg. daily. There was a generalized maculopapular erythematous rash with bullous formation, associated with severe constitutional disturbances; the condition subsided following treatment with cortisone and antibiotics. In a 74-month-old girl who was receiving sulphadimethoxine for otitis media a papular erythematous rash appeared after 9 days' treatment, the rash being extensive and similar to that in the first case. Antihistamines were effective in this patient. In a 5½-year-old girl who had been treated with sulphamethoxypyridazine in a dosage of 500 mg, daily for some weeks for a persistent urinary infection fever developed with a raised erythrocyte sedimentation rate and arthritis; 4 weeks after admission the L.E.-cell phenomenon was found in the blood. These manifestations slowly subsided after withdrawal of the drug, although 6 months elapsed before the L.E.-cell test became negative.

The authors briefly review the literature on the toxic effects, sometimes fatal, of these two drugs, which include skin eruptions (commonest), abdominal pain, arthralgia,

myalgia, blood dyscrasias, myocarditis, hepatitis, dizziness, and paraesthesiae. They conclude with the suggestion that these long-acting sulphonamides may precipitate an immunological response in a constitutionally abnormal reticulo-endothelial system, resulting in the development of lupus erythematosus. *Gerald Sandler*

ANTIBIOTICS

1329. Bacteriological and Pharmacological Properties of Phenoxybenzylpenicillin

I. M. Rollo, G. F. Somers, and D. M. Burley. British Medical Journal [Brit. med. J.] 1, 76-80, Jan. 13, 1962. 3 figs., 4 refs.

Since the discovery in 1959 of a method for the largescale production of the penicillin "nucleus", 6-aminopenicillanic acid, at least four oral penicillins with therapeutically useful properties have been synthesized. In the present paper the bacteriological and pharmacological properties of yet another penicillin chemically related to benzylpenicillin, phenoxymethylpenicillin, and penethicillin are described. This substance, phenoxybenzylpenicillin, which is the potassium salt of $6(\alpha$ phenoxyphenylacetamido)-penicillanic acid, has the high. solubility and very low toxicity of most other penicillins, is acid-resistant, although rather less so than phenoxymethylpenicillin, and can be given orally. Its antibacterial spectrum, minimum inhibitory concentration, and bacterial spectrum, minimum inhibitory concentration, and bactericidal activity against sensitive organisms in vitro are similar to those of phenoxymethylpenicillin and phenethicillin; it has almost exactly the same susceptibility to penicillinase as phenethicillin, but the blood level achieved with phenoxybenzylpenicillin is higher and more prolonged than the levels obtained with the two last-named penicillins. In three trials in 6 fasting subjects given each of these penicillins in turn a single dose of 125 mg, of phenoxybenzylpenicillin produced a mean peak blood level of $5.24 \mu g$. per ml., more than three times higher than that achieved with the same dose of phenoxymethylpenicillin and more than 2½ times higher than that with penethicillin. The highest concentrations were recorded half an hour after administration and substantial concentrations were still present after 4 hours in all subjects and in 40% after 6 hours. There were no detectable blood levels 6 hours after administration of either of the other penicillins nor after 4 hours in several subjects. Peak blood levels following administration of 125 mg. of phenoxybenzylpenicillin were higher than after 250 mg. of phenoxymethylpenicillin.

The pattern of the urinary excretion of phenoxybenzylpenicillin followed that of the other two penicillins, but the percentage of the dose excreted was less with phenoxybenzylpenicillin (23.8) than with phenoxymethylpenicillin (25.96) or penethicillin (33.3). Paper chromatography indicated that small amounts of two unidentified active components other than phenoxybenzylpenicillin were excreted, which was not the case with the other penicillins.

The results suggest that phenoxybenzylpenicillin should have advantages over existing oral penicillins and be effective at lower dose levels at longer time intervals.

A. Ackrovd

1330. Bacteriological and Clinical Studies with Phenoxybenzylpenicillin

M. J. CARTER and W. BRUMFITT. British Medical Journal [Brit. med. J.] 1, 80-82, Jan. 13, 1962. 2 figs., 3 refs.

A study of the bacteriological activity and clinical value of the new penicillin, phenoxybenzylpenicillin [see Abstract 1329], is reported from Edgware General Hospital, Middlesex, and St. Mary's Hospital, London. The antibacterial activity in vitro was intermediate between that of benzylpenicillin and that of phenoxymethylpenicillin. It had little activity against penicillinaseproducing strains of Staphylococcus aureus. Absorption and excretion tests-in 5 human volunteers given -125 mg. of phenoxybenzylpenicillin and 125 mg. of phenoxymethylpenicillin in turn by mouth 2 hours aftera light breakfast showed a mean peak blood concentra-- tion of 2.3 µg, per ml, one hour after phenoxybenzylpenicillin. This was about twice the concentration with phenoxymethylpenicillin. Levels approximately twice those obtained after 125 mg. of phenoxybenzylpenicillin were achieved with a dose of 250 mg., while after continuous administration of 125 mg. 6-hourly for 48 hours some cumulative effect was apparent. The new antibiotic was given in this last dosage to a group of patients. suffering from infective conditions—minor staphylococcal infections (7), acute sore throat due to Group-A strepto-. cocci (6), and one case each of gonorrhoea, pneumonococcal bronchopneumonia, pneumococcal sinusitis, anaerobic streptococcal puerperal pyrexia, and pyosalpinx. In all cases except that of pyosalpinx there was a prompt response as judged by clinical improvement. Good absorption from the intestinal tract was observed and blood levels of the antibiotic were satisfactory. No subjective or objective toxic symptoms or side-effects were A. Ackroyd reported.

1331. Penicillin and Erythromycin Singly and in Combination in Scarlatina Therapy, and the Interference between Them

J. STRÖM. Antibiotics and Chemotherapy [Antibiot. and Chemother.] 11, 694-697, Nov., 1961 [received Feb., 1962]. 6 refs.

At the Hospital for Contagious Diseases, Stockholm, 315 cases of uncomplicated scarlet fever were treated with (1) phenoxymethylpenicillin, (2) erythromycin, or (3) both drugs, and the results compared, there being 105 patients in each group. Therapy was begun on the second day and lasted 10 days, during which time daily tests for haemolytic streptococci in the nose and throat were carried out, follow-up tests being also performed 1 and 3 weeks after discharge. The dosage of the two drugs

varied according to age, that of phenoxymethylpenicillin ranging from 100,000 i.u. 3 times a day for 10 days for children aged 0 to 4 years up to 250,000 i.u. 3 times a day for those aged 15 years and upwards, while that of erythromycin ranged from 100 to 350 mg. 3 times a day for the same age groups.

In all groups streptococci disappeared after 6 days' treatment, but the proportion of cases in which organisms reappeared during treatment was 6% in Group 1, 22% in Group 2, and 9% in the combined-treatment group. (Group 3). After 3 weeks only 21% of patients in Group 1 still showed streptococci as compared with 36% of those in Group 2. Also the duration of fever was shorter (average 1.8 days) in Group 1 than in Group 2 (2.5 days). The erythrocyte sedimentation rate and the rise in antistreptolysin titre however were not significantly different in the 3 groups. Complications were few and mild. Lymphadenitis occurred in one case in Group 1, in 2 in Group 2, and in 4 in Group 3, bronchitis in one case in Group 1, and sinusitis in one case each in Groups 2 and 3; no case of nephritis occurred in any group. The electrocardiogram was abnormal in 6, 5, and 3 cases in the three groups respectively. The author concludes that penicillin alone was superior to both erythromycin and the two drugs combined. There was some evidence that erythromycin interfered with the bactericidal action of penicillin and he therefore recommends that the former drug should be employed only if penicillinase-producing staphylococci are also present. In such circumstances the combined therapy proved the more efficacious.

[This is a useful paper which confirms the value of penicillin alone in streptococcal infections, including scarlet fever, though the abstracter would personally favour the use of larger doses of penicillin for a shorter period, say, for example, 250,000 to 1,000,000 units 6-hourly for 48 to 72 hours.]

I. M. Librach

CHEMOTHERAPY OF TUMOURS

1332. Chemotherapy of Bronchogenic Carcinoma Utilizing Cardlac Catheterization

J. F. MORRIS and L. M. GOLDBERG. American Journal of the Medical Sciences [Amer. J. med. Sci.] 242, 527-533, Nov., 1961. 4 figs., 20 refs.

A technique of cardiac catheterization and pulmonary arterial injection of a chemotherapeutic drug in patients with bronchogenic carcinoma is described. At the Veterans Administration Hospital, Portland, Oregon, 18 patients with proven but previously untreated bronchogenic carcinoma received 0.6 to 1 mg. of nitrogen mustard per kg. body weight into the pulmonary artery via a cardiac catheter. Subjective or objective improvement was observed in 12 patients, with rapid and usually complete relief of chest-wall pain. There was less haematopoietic depression with this procedure than with intravenous infusion.

The authors state that the technique is suitable for cytotoxic agents which are rapidly inactivated.

G. Calcutt

1333. Clinical Observations on the Action of 1:6-Dimethanesulphonoxy-o-mannitol. [In English]

C. Sellei and S. Eckhardt. Acta medica Scandinavica [Acta med. scand.] 170, 511-516, Nov., 1961. 2 figs.; 3 refs.

This is a preliminary report from the National Cancer Institute, Budapest, of a trial of an anti-tumour agent, 1:6-dimethanesulphonoxy-p-mannitol (sulphonoxy mannitol), in the treatment of chronic myeloid leukaemia (13 cases) and other malignant conditions (52 cases). It was given intravenously in a dosage of 30 to 40 ml. per kg. body weight daily and, where necessary, intraperitoneally and into the pleural cavities. There were no ill effects from these routes of administration [no others were tried].

A full remission—that is, a return of the blood count to normal and disappearance of symptoms for more than 6 months—was obtained in 6 cases of myeloid leukaemia and a partial remission—lasting less than 6 months—in-4; in the remaining 3 cases of myeloid leukaemia there was subjective improvement only. In 2 cases, described in detail, a remission occurred in myeloblastic crisis, while in 2 others remission followed resistance to "myleran" (busulphan). [There is no record of the bone-marrow biopsy findings in these cases.] The authors note that the more mature the granulocytes, the less sensitive they are to sulphonoxy mannitol; they also maintain that patients become responsive again to myleran after treatment with sulphonoxy mannitol.

Subjective improvement only was noted in 11 of the 52 patients with malignant disease other than of the haematopoietic system. When large doses of sulphonoxymannitol were given a leukaemoid reaction occurred, with a leucocyte count of 30,000 per c.mm.; this ceased on withdrawal of the drug. Thrombocytopenia was noted in only 2 of the 27 cases in which the number of thrombocytes was estimated. [The time at which this occurred is not stated. The mean value of the erythrocyte and platelet counts in 11 of the patients with chronic myeloid leukaemia is recorded only for the 22 days of the treatment course.] Apart from the leukaemoid reaction and thrombocytopenia no other side-effects were observed.

The authors suggest that sulphonoxy-mannitol is a promising therapeutic agent in chronic myeloid leukaemia, especially when myleran is ineffective or a myeloblastic crisis occurs.

J. S. Malpas

1334. High-dose Nitrogen Mustard Therapy with Intermittent Aortic Occlusion

J. K. Duff, J. Dennis, R. A. Cliff, P. Clifford, and H. F. Oettgen. *British Medical Journal [Brit. med. J.*] 2, 1523–1528, Dec. 9, 1961. 1 fig., 15 refs.

Nitrogen mustard (mustine hydrochloride; HN2) is an alkylating agent used in cancer therapy. Alkylating agents interfere with tissue growth by reacting with cellular nucleic acids. This effect is not tumour-specific, but affects all growing tissue. Of normal tissues, bone marrow, lymph nodes, and intestinal epithelium are chiefly affected, the most important manifestation of toxicity being bone-marrow depression. The tolerance dose is that from which bone marrow can recover.

Therefore attempts have been made to raise the concentration of the agent in tumour tissue without increasing the amount in bone marrow and these have included: (1) local injection into malignant effusions; (2) administration into the artery supplying the tumour; (3) regional perfusion by temporary exclusion of the tumour area from the general circulation; and (4) systemic administration with protection of the bone marrow by (a) removal and storage of part of it for replacement afterwards; and (b) temporary and intermittent occlusion of the abdominal aorta. In performing Procedures 3 and 4b it is essential to remember that HN2 is active in the circulating blood for less than 10 minutes.

In this paper the technique employed for Method 4b as used at King George VI Hospital, Nairobi, is described. With the patient under relaxant anaesthesia, a 15×15 -cm. sandbag is first put on the abdomen and a larger sandbag (23 × 46 cm.) then laid across the first, the whole being bound tightly with an Esmarch bandage around the bags, patient, and table so as to compress the aorta against the. lumbar spine, thus occluding most of the collaterals. When femoral arterial pulsation ceases, indicating satisfactory occlusion, one-quarter of the total dose of HN2 (1.2 to 2 mg, per kg, body weight) is given into an arm vein over 2 minutes in a concentration of 1 mg. per ml. of 0.9% saline, the second quarter being injected after 10 minutes: at the end of 20 minutes the sandbags are removed and the tourniquet is released. The second half of the total dose is given within 48 hours by the same procedure.

So far 10 patients with inoperable cancer above the diaphragm have been treated. In 9 there was adequate protection of the pelvic bone marrow against a dosage of HN2 of up to 3 mg. per kg. body weight. Two patients showed symptoms suggestive of 8th nerve damage. Nausea, vomiting, and anorexia occurred in all cases. but there was no instance of gastro-intestinal damage. Other side-effects included alopecia in 3 patients and mental confusion in a further 3. There was a remarkable response in 3 cases of carcinoma of the post-nasal space and in one of carcinoma of the oesophagus, there being complete tumour regression and later negative findings in a biopsy specimen from the former site of the tumour. It is concluded that the results of this method of treatment justify further studies. I. G. Williams

1335. Cyclophosphamide in Children with Cancer D. PINKEL. Cancer [Cancer (Philad.)] 15, 42-49, Jan.Feb., 1962. 5 figs., 12 refs.

Thirty-three children with advanced, inoperable solid tumors were treated with cyclophosphamide, an alkylating agent derived from mechlorethamine (nitrogen mustard). Temporary symptomatic relief and tumor regression were observed in 3 of 8 children with neuroblastoma, 3 of 7 with rhabdomyosarcoma, 1 of 4 with osteogenic sarcoma, 1 of 2 with Ewing's sarcoma, 1 of 2 with malignant presacral teratoma, and 1 with an undifferentiated sarcoma of the axilla.

Toxic effects included anorexia, nausea, emesis, diarrhea, mucosal ulceration, leukopenia, and alopecia. A syndrome of dysuria, hematuria, and mild proteinuria

was observed in 5 patients and was thought to represent toxic cystitis. Significant thrombocytopenia occurred in 2 patients but was not associated with bleeding tendency.—[Author's summary.]

1336. Clinical Experience with Cyclophosphamide in. **Malignant Disease**

D. A. L. DICK and A. F. PHILLIPS. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 974-986, Oct. 28, 1961. 1 fig., 40 refs.

The effects of cyclophosphamide were studied at the Cancer Clinic, Edmonton, Canada, in 67 patients, most of whom had confirmed advanced malignant disease. The drug was given initially in doses of 100 mg, intravenously, followed by 200 mg. daily, irrespective of height and weight, for 5 days each week. Later these patients received a total of 5 g. in 4 weeks given on 6 or 7 days of each week, continuing to a higher dosage if this was well tolerated and a favourable response obtained. After 1 to 3 weeks many continued as out-patients taking the drug orally in doses of 200 mg. daily. Side-effects were nausea, alopecia, and depression of the bone marrow. Nausea occurred in 60% and vomiting in 22% of the patients: In 36% of the patients there was some hair loss, with complete alopecia in only 4 cases, in which regrowth of the hair was complete in 3 months. Cyclophosphamide depresses the platelet count less than nitrogen mustard and other alkylating agents. In 19 cases the leucocyte count fell to less than 2,000 per c.mm., but in only 3 cases did the platelet count fall below 100,000 per c.mm. and it rapidly returned to normal when the treatment was stopped. The degree of leucocyte and platelet depression is related to the degree of bone-marrow involvement, the extent of liver disease, and previous chemical and radiation treatment.

In multiple myeloma there was a higher incidence of leucopenia during treatment with cyclophosphamide than in other reticuloses so treated. There was a good response in 5 patients out of 7, in one of whom there was recalcification of lesions in the ribs and elsewhere. Of 2 patients with Ewing's sarcoma who showed a good subjective response, one was well 7 months later. The · disease was arrested in 3 out of 5 cases of carcinoma of the large intestine treated with local irradiation and cyclophosphamide. The same combination, used postoperatively, of local irradiation with cyclophosphamide showed encouraging results in 2 out 4 patients with carcinoma of the ovary. The treatment of hypernephroma gave some temporary relief to the 6 patients treated and sufficient response in 3 of them to warrant further trials of cyclophosphamide combined with radiotherapy for this condition. No beneficial results were obtained in 3 cases of lymphosarcoma, 3 of adenocarcinoma of the stomach, 4 of reticulum-cell sarcoma, one of skin cancer, 2 of lympho-epithelioma, and one case each of pleural mesothelioma, carcinoma of the tongue, carcinoma of the bladder, and carcinoma of the cervix. Variable results were obtained in 6 cases of hypernephroma and 9 of carcinoma of the lung.

The authors suggest that a combination of radiotherapy and cyclophosphamide (1.4 g. weekly) might be used in

malignant disease not usually amenable to irradiation alone, but they have found that liver and lung metastases are rarely benefited. As the effect of this drug is unpredictable and slow, it should not be used when effectiveagents already exist and it is contraindicated in conditions requiring urgent treatment, such as, for example, superior vena caval obstruction. Anne Tothill

1337. Cyclophosphamide in Treatment of Disseminated Malignant Disease

C. J. Anders and N. H. Kemp. British Medical Journal. [Brit. med. J.] 2, 1516-1523, Dec. 9, 1961. 5 figs., 13 refs.

At St. George's Hospital, London, 92 patients with widespread malignant disease considered to be beyond the scope of conventional treatment have been treated with the alkylating agent cyclophosphamide ("endoxan", "cytoxan") since November, 1959. The drug was given intravenously first in a test dose of 100 mg, and thereafter usually in a dosage of 200 mg. daily; in a few exceptional cases up to 400 mg. was given. In each case the dosage was regulated by the effect on the haematopoietic system, a deliberate attempt being made to reduce the total leucocyte count to 2,000 per c.mm. This required 7 to 14 days, after which oral doses of 100 to 200 mg, daily were given in divided doses to maintain the total count at between 2,000 and 3,000 per c.mm.; when stabilization was obtained treatment was continued on an out-patient basis. The results were judged both objectively and subjectively.

For various reasons only 76 patients were available for assessment. Of 20 with carcinoma of the breast objective improvement was recorded in 6 and subjective improvement in 3. Among 27 patients with carcinoma of the bronchus the corresponding figures were 8 and 1, and for 14 with malignant lymphoma they were 7 and 2 respectively. Two patients with multiple myelomatosis experienced lessening of bone pain, but there was no radiological improvement. The remainder consisted of single cases mainly of carcinoma of various organs. In regard to side-effects alopecia occurred in 60% of the patients after 3 to 4 weeks, and in one-quarter of the total baldness was complete; new hair which grew was stunted, and a wig had to be worn. The other frequent side-effect was bone-marrow failure. If this occurs and the patient survives the leucocyte count usually recovers spontaneously within 4 to 7 days of withdrawal of the drug-" an undoubted advantage of cyclophosphamide". Of 28 patients in whom the leucocyte count fell below 1,000 per c.mm. 5 died from marrow aplasia and overwhelming infection. The incidence of nausea and vomiting depended upon the dosage and was less than with comparable doses of cytotoxic drugs. Discussing survival the authors state that the long-term results were not encouraging. In only 7 patients was objective improvement maintained for longer than 6 months, a further 3 obtaining subjective improvement for the same period. However, 2 patients with carcinoma of the breast responded for more than one year and one of these has remained symptom-free after 18 months.

I. G. Williams

Infectious Diseases

1338. Infections with Parainfluenza Viruses in Children with Respiratory Illnesses in Holland

J. Van Der Veen and F. A. A. M. Smeur. American Journal of Hygiene [Amer. J. Hyg.] 74, 326-331, Nov., 1961. 18 refs.

In a study of the significance of infection due to parainfluenza viruses in acute respiratory illness in children complement fixation and haemagglutination inhibition tests were carried out on children admitted to St. Elisabeth Hospital, Tilburg, Holland, between February, 1959, and November, 1960, the ages of the children and of 50 controls ranging from 3 months to 14 years. Paired sera were tested against Sendai virus and parainfluenza viruses Types 1, 2, and 3. The two laboratory tests were considered to be equally effective in detecting the development of antibody.

Of 245 children suffering from disease of the respiratory tract 11 4% showed evidence of infection with parainfluenza virus. In 57% of the cases of croup and 8.5% of the cases of pneumonia there was associated infection with the virus. In 8 cases an antibody response was obtained to both para-influenza virus Type 1 and parainfluenza virus Type 3. All the patients were serologically negative for adenovirus infection and influenza A and B, psittacosis, and Q-fever viruses. Tests for cold agglutinins gave negative results.

An increase in antibody titre against Sendai virus occurred in patients with antibody response to parainfluenza virus but not in patients giving a negative response to the latter. It would appear, therefore, that Sendai virus was not a cause of infection in the cases under observation.

A. Garland

1339. E.C.H.O. Type 9 Infection in 1960: a Study in General Practice

J. B. LANDSMAN and E. J. BELL. British Medical Journal [Brit. med. J.] 1, 12–16, Jan. 6, 1962. 10 refs.

Virological studies were carried out during an outbreak of a rubella-like illness in northern Glasgow in the summer of 1960. Each case was notified by the general practitioner and the household concerned was visited within 24 hours. Throat swabs and specimens of faeces were collected for virus isolation from all members of the household and samples of blood were taken from some for serological examination. After excluding three families in which the illness could be ascribed to other causes there remained 20 families with a total of 80 individuals who were observed for 10 to 14 days, details of any illnesses being recorded. Evidence of infection with E.C.H.O. virus Type 9 was obtained in 18 families by virus isolation; in one other family the diagnosis of such infection was based on a rise in antibody titre. Of the 80 subjects 43 reported sick, of whom 31 were children. A rash was observed on 23 of the children and was seen as either minute discrete papules, pink or colourless, or as larger, maculopapular areas, pink or red.

Only one of 12 adults had a rash. Headache and vomiting were common presenting symptoms at all ages. Enlargement of cervical lymph nodes was noted in 21 patients, mostly children. In the majority of cases the illness was mild and lasted 4 to 5 days; in one child, however, aseptic meningitis developed. In adults muscular aches and headache suggested "influenza". Symptomless infection occurred, as demonstrated by the isolation of the virus from 5 out of 14 throat swabs and one out of 2 rectal swabs from unaffected individuals.

[In view of the similarity of the illness to rubella, it is a little surprising that there is no comment on the presence or absence of occipital lymph-node enlargement.]

J. E. M. Whitehead

1340. Contribution to the Study of the Epidemiology of Viral Hepatitis. Serum Transaminase Determination and the Common Liver Function Tests in a Study of Anicteric Forms of the Disease. (Contributo allo studio dell'epidemiologia dell'epatite virale. Il dosaggio delle transaminasi seriche e le comuni prove di funzionalità epatica per la ricerca delle forme anitteriche della malattia) F. GIANNELLI, P. C. ANICETI, and A. DORIA. Annali Sclavo [Ann. Sclavo] 3, 638-658, Nov.-Dec., 1961 [received Feb., 1962]. 38 refs.

An outbreak of viral hepatitis affecting 35 of 60 healthy inmates of a home for children whose parents were suffering from tuberculosis, and 2 adults out of a staff of 26, afforded an opportunity to investigate the serum transaminase levels, liver function, and any changes in the serum proteins in these subjects. A rise in serum transaminase activity indicates parenchymal liver damage. Of the 37 patients 26 (70.3%) showed an anicteric form of the disease, which in 15 cases (43%) was symptomless. In 4 non-icteric patients changes in the serum transaminase values were noted many days before any clinical symptoms became manifest, in one case such change preceding onset of the disease by as much as 49 days. The authors suggest that the serum transaminase level should be determined in all clinically suspect cases of hepatitis and in the families of such patients, and that all verified or suspect cases should be isolated or admitted to hospital and discharged only when the transaminase level has become normal. Franz Heimann

1341. Early Recognition and Therapy of Disseminated Coccidioidomycosis

J. A. COLWELL and S. P. TILIMAN. American Journal of Medicine [Amer. J. Med.] 31, 676–691, Nov., 1961. 11 figs., 19 refs.

Coccidioidomycosis was diagnosed in 50 patients observed at Davis-Monthan Air Force Base, Tucson, Arizona, between August, 1956, and July, 1959.

Primary pulmonary involvement was diagnosed in 42 patients who satisfied one or more of the following criteria: (1) conversion of the 1:100 coccidioidin intra-

dermal test-within 21 days of onset of symptoms (15 patients); (2) a complement fixation titre of at least 4 plus in 1:2 dilution but not greater than 1:16 or a precipitin titre of 4 plus in any dilution (10 patients); and, (3) clinical course (one patient). The average age of the patients in this group was 29 (range 6 to 50) years; 34 were males and 4 were negroes. Nine gave a history of excessive exposure to dust. All had lived in an endemic area for an average of 28 months (range 1 to 132 months). No deaths occurred. Chest pain, chiefly pleuritic, was the main symptom, the average duration of which was 4 days. The main radiological finding was pulmonary infiltration of the left lower lobe (17 cases). Hilar enlargement was present in 50% of cases. Serial radiography showed complete resolution in 11 cases and granu-· loma formation in 24. The patients were followed up for 52 weeks without evidence of dissemination.

The disseminated form of the disease was diagnosed in patients who satisfied one or both of the following criteria: (1) a maximum complement fixation titre of 1:32 or greater (6 of 7 patients tested); and (2) isolation of Coccidioides Immitis from an extrapulmonary site (7out of 7 patients tested). The average age of these patients was 23 (range 19 to 32) years; 7 were males and 5 negroes. A history of excessive exposure to dust was obtained in 6 cases. All 8 patients had lived in an endemic area for an average of 13 (range 41 to 30) months. They were followed up for 40 to 155 weeks. There was one death-that of a negro woman aged 20 years with septicaemia who died after 5 days. The onset of the illness was gradual, weight loss and malaise being the chief symptoms (average duration 10 days). The main radiographic findings in the chest were hilar adenopathy (6 cases), and infiltration (7 cases); one patient had cardiomegaly. Slow clearing occurred in all cases after 4 weeks. Temperature elevation, weight loss, anaemia, and extrapulmonary findings (skin, septicaemia, meningitis, peritonitis, lymphadenopathy) were common in this group. No remarkable differences in respect of the leucocyte count or erythrocyte sedimentation rate (E.S.R.) were found between the two groups.

Treatment was symptomatic in 26 of the primary cases; 12 had penicillin and 4 had other antibiotics. In the disseminated group 6 patients were given amphoteric in B for 5 to 41 weeks with good to excellent results in 5. The total dosage ranged from 1.15 to 6.39 g. Reversible renal abnormalities, as judged by a raised blood ureal level, urinary casts, and abnormal phenolsulphonphthalein excretion, were the main toxic effects.

The authors emphasize that negro patients with a history of more than one week's illness in which the chief symptoms are those of systemic disease with weight loss are particularly to be suspected of disseminated coccidioidomycosis. A presumptive diagnosis can usually be made by careful evaluation at the 4th week, but definite diagnosis depends on demonstration of the organism in an extrapulmonary site. Reaction to 1:100 coccidioidin injection intradermally becomes positive at the time of the first extrapulmonary spread. An elevated E.S.R. is no contraindication to discharge from hospital. Treatment with amphotericin B is effective if the dosage and duration of treatment are adequate.

I. M. Librach

1342. Sarcoidosis (Besnier-Boeck-Schaumann Disease) and Trauma. (Sarkoidose (Morbus Besnier-Boeck-Schaumann) und Trauma)

G. JÜRGENSEN. Deutsches Archiv für klinische Medizin [Dtsch. Arch. klin. Med.] 207, 431-455, 1961. 8 figs., bibliography.

In order to assess the role of trauma in the aetiology Boeck's sarcoid the author, working at the Institute of Human Genetics, Göttingen, has reviewed the records of 600 cases of sarcoidosis admitted to hospital in West Germany and West Berlin. In 10 there was a history of trauma and 7 of these patients had sarcoid of the lung, 6 of them having received thoracic injuries in the war of 1939-45. The time between the injury and discovery of sarcoid ranged from 3 to 33 years, with an average of 13 years. In no case did the sarcoidosis first appear anywhere near the site of injury, but always in the hilar lymph . n nodes. The 7th patient with sarcoid of the lung had a sister who also suffered from pulmonary sarcoid, but she had sustained no chest injury. The remaining 3 patients all had generalized sarcoidosis, but developed sarcoid lesions in the scars of old injuries or operation wounds. Here, too, many years elapsed between the injury and appearance of the disease.

In view of these findings and evidence from earlier reports in the literature the author concludes that trauma plays no significant part in the development of sarcoidosis.

D. Goldman

1343. Mycobacterial and Mycotic Antibodies in Sera of Patients with Sarcoldosis: Results of Studies Using Agar Double-diffusion Technique

J. S. CHAPMAN. Annals of Internal Medicine [Ann. intern. Med.] 55, 918-924, Dec., 1961. 3 figs., 21 refs.

Sarcoidosis has been pronounced "a disease of unknown actiology", though this view is not universally accepted. In the present study the author has sought precipitins against anonymous mycobacterial antigens in sera obtained from patients with sarcoidosis. Although the investigation was carried out at the University of Texas Southwestern Medical School, Dallas, sera were obtained from many parts of the U.S.A. and from Europe. The technique employed was the simple one of agar-gel diffusion, in which serum was allowed to interact with 5 different antigens prepared from photochromogenic, non-photochromogenic, and scotochromogenic anonymous mycobacteria, and also against antigens prepared from the human strain of tubercle bacilli as well as from Histoplasma capsulatum, Cryptococcus neoformans, Blastomyces, and Coccidioides Immitis.

Of the 112 sera studied 88 (78%) showed precipitins against anonymous mycobacteria, 9 against Mycobacterium tuberculosis, 5 against Histoplasma, 4 against cryptococcal antigen, and 2 against blastomycotic antigen. Sera from recently developed cases of sarcoidosis showed reactions with greater frequency and with more bands than did older cases. The significance of these findings is not yet clear, but the differences revealed suggest that agar-gel diffusion, together with the clinical findings, may be of diagnostic value.

D. Geraint James

Tuberculosis

1344. I. Diagnosis of Tuberculous Meningitis in the Adult. (I. Diagnostic de la méningite tuberculeuse de l'adulte)

J. Pernod, C. Chambatte, and J. Battme. *Poumon et le cœur [Poumon]* 17, 623-634, Sept.-Oct., 1961 [received Jan., 1962]. 2 figs.

In this study the authors' purpose was to analyse the different elements of diagnosis by reviewing their observations on 80 cases of tuberculous meningitis treated at the Percy Military Hospital since 1953. Only 3 of the patients were over the age of 30, the remainder being between 19 and 30 years of age. After a brief review of the various forms of onset, attention is directed to the importance of the findings obtained by means of lumbar puncture, with particular emphasis on the search for tubercle bacilli in the cerebrospinal fluid. These organisms were identified directly in only 29 of the 80 cases and by culture or guinea-pig inoculation in a further 26, a total of 55. The value of the study of previous illnesses and clinical and supplementary examinations is stressed. In 48 (60%) of the cases the diagnosis was made within 10 days of onset and in this group there were no deaths. Of the remaining 32 patients 3 (10.4%) died.

, Norman F. Smith

1345. II. Therapeutic Results in Tuberculous Meningitis in the Adult since the Introduction of Isoniazid. (II. Résultats thérapeutiques de la méningite tuberculeuse de l'adulte depuis l'utilisation de l'isoniazide)
J. Pernod, C. Chambatte, and J. Batime. Poumon et le cœur [Poumon] 17, 635-651, Sept.-Oct., 1961 [received Jan., 1962]. 2 figs., 44 refs.

In the second part of this study [see Abstract 1344] the necessity for intrathecal therapy and the influence of hormone (steroid) treatment are considered. In the · light of their experience the authors conclude that intrathecal therapy is not necessary in the usual forms of tuberculous meningitis in the young adult. Hormone therapy, they consider, should be given early and mainly for the greater comfort of the patient and the suppression of clinical signs, rather than for the marked reduction in mortality or incidence of complications which it may confer. A follow-up study for up to 7 years showed a mortality of 5% (4 deaths). Among the 76 survivors no seque ae were found in 51%, minimal sequelae in 35.5%, and important sequelae in 13%. These results are related to the different types of treatment employed and they emphasize the importance of isoniazid in high dosage given systemically without intrathecal adminis-

Apart from physical sequelae the importance of the psychological factor in achieving rehabilitation is stressed. Of 65 patients followed up 34 were able to resume an occupation.

[A careful and detailed study.] Norman F. Smith

DIAGNOSIS AND PROPHYLAXIS

1346. Epidemiological Evidence of the Presence of Nontuberculous Sensitivity to Tuberculin in Queensland E. W. ABRAHAMS and H. SILVERSTONE. *Tubercle* [*Tubercle* (*Lond*.)] **42**, 487–499, 1961. 23 refs.

Tuberculin surveys with human tuberculin in Australia have in recent years shown a larger proportion of positive tuberculin reactors among school-children aged 13 and 14 in North and Central Queensland than in other areas of the Dominion. The notification rates for tuberculosis both for age groups under 14 and over 14 years are almost twice as great in Queensland as in the more southerly State of Victoria, but the ratio of juvenile to adult cases of tuberculosis is the same in Queensland as in Victoria, suggesting a 4-fold infection rate in the former. The authors state that the latter finding may indicate that infection by other than mammalian strains of Mycobacterium tuberculosis occurs in Queensland, similar to that in other warm and tropical areas reported by Nyboe (Bull. Wld Hlth Org., 1960, 22, 5) and other workers. In view of this, Mantoux or Heaf tests on school-children were carried out with standard old tuberculin (P.P.D.-S.) and also purified protein derivatives of the following organisms: Battey strain (P.P.D.-B.), Myco. fortuitum, "vellow bacillus", a Nocardia species, and avian tuberculin (P.P.D.-A.).

A smaller incidence of manifest tuberculous disease was found among those children shown to be highly sensitive to tuberculin than was expected. In all but one of the areas in Queensland investigated reactions to P.P.D.-B. were more frequent than reactions to P.P.D.-S., while in the remaining area the reverse was the case. In general, there was good agreement between the reactions produced by avian (P.P.D.-A.) tuberculin and old tuberculin, while the reaction rate with P.P.D.-A. was higher than with Standard P.P.D.-A. The reaction patterns to yellow bacillus and Myco. fortuitum P.P.D. were similar to that to P.P.D.-S. In a discussion of the practical implications of these findings it is suggested that in Queensland and other areas of similar climate dependence upon a single simple tuberculin test with a low dose of tuberculin would now appear to be inadequate. T. M. Pollock

1347. Liquid or Freeze-dried B.C.G. Vaccine: Persistence of Tuberculin Sensitivity in Schoolchildren after Vaccination

C. L. MILLER and B. J. KINSLEY. British Medical Journal [Brit. med. J.] 2, 1322–1324, Nov. 18, 1961. 4 refs.

In this paper from the Medical Research Council, London, a study is reported of the persistence of tuberculin sensitivity 4 years after vaccination. In 1957 (Brit. med. J., 1958, 1, 79; Abstr. Wld Med., 1958, 24, 173) two groups of children (aged 13 to 14 years) were vaccinated with either Danish liquid B.C.G. or British freeze-dried

B.C.G. vaccine. Tuberculin tests 3 months and one year later showed that there was little change in tuberculin sensitivity. The same subjects were retested 4 years later, each being given 3 t.u. In the group given the liquid vaccine the percentage positive to 3 t.u. declined from 98 to 81, while in the group given the dried vaccine the corresponding figures were 93 to 71.

T.-M. Pollock

1348. BCG Vaccination by Multiple Puncture: Preliminary Report

A REPORT FROM THE RESEARCH COMMITTEE OF THE BRITISH TUBERCULOSIS ASSOCIATION. Tubercle [Tubercle (Lond.)] 42, 413–427, 1961. 15 refs.

The post-vaccination tuberculin sensitivity after B.C.G. vaccination by multiple puncture has been studied in 898 school-children in Lancashire and 866 in Salford, a total of 1,764. Two strengths of B.C.G. vaccine were employed, namely, 70 mg. per ml. and 100 mg. per ml., and with each strength three types of multiple-puncture apparatus containing 6, 20, or 40 needles respectively were used. There were thus 6 groups of children in the investigation, allocation to the groups being by random selection.

All the children tested in Lancashire and over 90% of those in Salford were tuberculin sensitive, as shown by a Heaf test 10 to 13 weeks after vaccination. In Lancashire the children in the group given the 70 mg. per ml. vaccine by the 20-needle apparatus showed stronger tuberculin sensitivity than those vaccinated with the 6-or 40-needle apparatus; no differences in degree of sensitivity were observed in the corresponding 3 groups in Lancashire given the 100 mg. per ml. vaccine. In contrast, among the children in Salford given the 70 mg. per ml. vaccine the degree of tuberculin sensitivity was not affected by the number of needles employed, but of the 3 groups receiving the 100 mg. per ml. vaccine, that vaccinated with the 6-needle apparatus showed a lower degree of sensitivity than did the other two groups.

One year after vaccination further tests revealed that tuberculin sensitivity was lower than that at 10 to 13 weeks in Salford and very considerably lower in Lancashire. It is suggested that the difference in the two areas, both in post-vaccination tuberculin sensitivity and in vaccination lesions and minor complications, may have been due to differences in pressure release of the multiple-puncture apparatus used in the different areas. It is concluded that the 20-needle gun appeared to be the most satisfactory, provided the depth of skin penetration was adequate, but further work on multiple puncture B.C.G. vaccination is required.

T. M. Pollock

1349. Effect of Prednisolone on the Tuberculin Test and on the Middlebrook-Dubos Test: a Comparative Inquiry into the Existing Relationship between the Variations Observed. [In English]

C. STEPHANOPOULOS and D. KAMAROULIAS. Acta tuberculosea et pneumologica Scandinavica [Acta tuberc. pneumol. scand.] 41, 19-27, 1961. 25 refs.

The authors stress the variable and even opposite results achieved by various investigators who have studied the effect of steroids on the tuberculin test and on the serum antibodies. The present study was undertaken at the Seamen's Chest Hospital, Penteli, Athens, to determine the effect of prednisolone on the tuberculin (Mantoux) test and on the serum antibodies in tuberculous patients and also the correlation between these two tests, a total of 20 patients with exudative disease and cavitation being investigated. The dosage of prednisolone was high, starting with 40 mg. daily for 30 days. For the Mantoux test purified tuberculin P.P.D. was employed, and the study of the antibodies was made by the Middlebrook—Dubos agglutination test as modified by Smith and Scott (Amer. Rev. Tuberc., 1950, 62, 121).

Of the 20 patients investigated, 12 showed no change in the Mantoux test result, while the other 8 changed to increased positivity or increased negativity. In regard to antibodies half the patients exhibited no change and in those who did the variations were slight and not statistically significant. Moreover, there appeared to be no correlation between the Mantoux test changes and the antibody titre. It is concluded that these results throw doubt on the role of the antibodies in causing conversion in the Mantoux test and might be held to emphasize the difference between tuberculous allergy and humoral immunity.

Paul B. Woolley

RESPIRATORY TUBERCULOSIS

1350. Single-breath Pulmonary Diffusing Capacity Measurements in Patients with Pulmonary Tuberculosis F. Dietiker, W. Lester, R. Gottlieb, and B. Burrows. *American Review of Respiratory Diseases [Amer. Rev. resp. Dis.]* 84, 807–813, Dec., 1961. 4 figs., 4 refs.

The results of breath-holding diffusing capacity tests performed on 221 patients with pulmonary tuberculosis are reported from the Suburban Cook County Tuberculosis Hospital-Sanitarium, Hinsdale, Illinois. The diffusing capacity showed a definite inverse relationship with age and correlated well with the lung volume. The diffusing capacity per litre of lung volume was within normal limits in most of the patients, it being low in those with pulmonary emphysema. It was also low in male patients over 50 years of age. No correlation was found with other factors, and it is concluded that routine determination of single-breath diffusing capacity in patients with pulmonary tuberculosis adds little useful information to that obtained from ventilation and nitrogen-washout studies. The "alveolar-capillary block" syndrome is not characteristic of any of the common forms of this disease. G. M. Little

1351. The Diffusing Capacity of the Lung in Acute Pulmonary Tuberculosis

M. H. WILLIAMS JR., N. S. SERIFF, T. AKYOL, and OK HI YOO. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 814–817, Dec., 1961. 1 fig., 5 refs.

A bedside method for measuring the single-breath diffusing capacity of the lung in patients acutely ill with tuberculosis is described from the Albert Einstein College of Medicine and the Bronx Municipal Hospital Center, New York. This is a modification of the breath-holding technique developed by Ogilvie et al. (J. clin. Invest., 1957, 36, 1): [For details the original paper should be consulted.] The measurement is said to be easy to perform and highly reproducible. Estimations were made on 35 patients suffering from acute tuberculosis, none of whom had severe anaemia, which may cause reduction in diffusing capacity. The extent of radiological abnormality, as assessed by 3 separate observers, was found to compare poorly with the reduction in vital capacity, but there was good correlation between radiological involvement and the impairment of diffusion as shown by the test.

The authors suggest that the diffusing capacity may be a more sensitive and accurate index of the extent of lung involvement in cases of pulmonary tuberculosis than the radiograph.

G. M. Little

1352. The Use of Hypertonic Aerosol in Production of Sputum for Diagnosis of Tuberculosis: Comparison with Gastric Specimens

N. M. Hensler, C. G. Spivey Jr., and T. M. Dees. Diseases of the Chest [Dis. Chest] 40, 639-642, Dec., 1961. 6 refs.

The authors found that 30% of the patients admitted for diagnosis to the tuberculosis section of the U.S. Air Force Hospital, Scott Base, Illinois, were unable to produce adequate sputum for bacteriological examination. They therefore tried giving an inhalation of a hypertonic aerosol solution at a temperature of approximately 105° F. (40.6° C.) inhaled from a distance of 4 to 6 inches (10 to 15 cm.). At the beginning of the experiment a 10% solution of sodium chloride in 20% propylene glycol was used, but later the saline content was reduced to 5%. Cultures were grown both on Loewenstein-Jensen and Middlebrook media. It was found that a greater number of positive cases were identified from specimens of sputum than from gastric specimens. It is suggested that this method deserves further investigation. Franz Heimann

1353. The Prevalence of Drug-resistant Strains of Myco-bacterium tuberculosis Isolated from Untreated Patients in New York City during 1960

A. D. CHAVES, G. DANGLER, H. ABELES, A. B. ROBINS, and D. WIDELOCK. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 84, 647-656, Nov., 1961.

Because of recent reports in the world literature suggesting that there has been a definite increase in the prevalence of strains of *Mycobacterium tuberculosis* resistant to isoniazid among patients with undiagnosed disease and so never treated with antituberculous drugs, the authors, working in the Department of Health, New York City, planned the study reported in this paper, in which all major hospitals and 25 tuberculosis clinics in the city took part. The techniques of culture and assessment of sensitivity to streptomycin, isoniazid, and PAS were the same as those used in 1952, 1954, and 1955, thus affording a unique opportunity for comparison. Of the strains isolated from 428 newly discovered and

previously untreated patients in New York City during 1960 59 (13.8%) showed some degree of isoniazid resistance (compared with 6.5% in 1955), while 22 strains (5.1%) exhibited some degree of streptomycin resistance, a result similar to that found in 1955. Resistance to PAS was found in 9 strains (2.1%). On the basis of the criteria for admission to the study the prevalence of significant isoniazid resistant "patient-strains" was 2.6% in 1960 compared with approximately 1% in 1955, though there was no significant difference in the numbers showing resistance to streptomycin and PAS in the 2 years. The authors emphasize the necessity for successful treatment of newly diagnosed and untreated tuberculosis and adequate isolation and supervision of patients with drug-resistant disease.

W. Raymond Parkes

1354. Isoniazid in Primary Tuberculosis in Infancy: a Controlled Clinical Trial

J. LORBER. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 669-686, Dec., 1961. 31 figs., 9 refs.

All tuberculin-positive infants with uncomplicated and previously untreated primary pulmonary tuberculosis seen at the Department of Child Health, Sheffield University, from April, 1952, to October, 1955, were enrolled in a prospective investigation to assess the value of specific antituberculous therapy. Of 59 such infants aged 2 years or under, 30 received isoniazid in a dosage of 5 mg. per kg. body weight daily together with PAS (500 mg., per kg. daily) for 3 months, the remaining 29 receiving no specific chemotherapy. The average age of the "treated" infants on admission to the investigation was 16 months and that of the "controls" 13 months; thus the control group was weighted with small infants, but some of the treated group had respiratory symptoms such as stridor. Initial radiological appearances were similar in the two groups.

Tuberculous complications observed in the treated group included miliary spread (one case), bronchial obstruction (3), osteitis (1); and in the control group meningitis (1), bronchial obstruction (1), and osteitis (1). (Some of the complications recorded in the treated group were in fact present before chemotherapy was started.) The general health of the infants as judged by gain in weight and by incidence of non-tuberculous illnesses such as measles, whooping cough, and bronchitis was similar in the treated and control groups. Serial radiographs in the two groups were similar in respect of degree of shadowing and the appearance of calcification.

The author concludes that "this investigation failed to indicate that isoniazid associated with PAS conferred any demonstrable benefit on infants suffering from uncomplicated primary tuberculosis".

[This conclusion is at variance with the experience of Mount and Ferebee (New Engl. J. Med., 1961, 265, 713; Abstr. Wld Med., 1962, 31, 175), who gave isoniazid for 12 months to 1,394 children with primary tuberculosis and compared their progress with 1,356 children not given specific chemotherapy; these authors concluded that isoniazid not only reduced the local lung complications but prevented haematosenous spread from the primary lesion.]

R. M. Todd

Tropical Medicine

1355. Growth and Mortality in Children in an African Village

I. A. McGregor, W. Z. Billewicz, and A. M. Thomson. British Medical Journal [Brit. med. J.] 2, 1661–1666, Dec. 23, 1961. 3 figs., 19 refs.

The authors report a survey of growth and mortality in African children in a village on the Gambia river. The community studied consists of about 700 inhabitants who live in mud or wooden huts. They grow their own food crops-rice, millet, sorghum, maize, findo (Digitaria sp.), and groundnuts. Although goats and cattle are kept and fish is abundant in the river, neither dairy produce nor fish is consumed to any great extent. Infants are exclusively breast-fed for the first 4 to 6 months of life and then supplements of rice, millet or sorghum, fish, groundnuts, and greenleaf sauces are added until the child is receiving a diet of adult pattern. Breast-feeding is finally stopped at 18 to 22 months. Births and deaths have been registered by a reliable literate native from 1950 onwards and a branch of the Medical Research Council Laboratories has been stationed in the area since 1949. A preliminary survey in 1950 showed that malaria was hyperendemic, with a parasite rate for all ages of 54.7%. Wuchereria bancrofti was found in 36% and trypanosomes in 2.5% of the population. Hookworm is prevalent and all attempts to control the infection have failed.

During the 5 years 1949-53 197 babies were born, of whom 187 remained in the village and available for study. Of these, 81 (43%) died before reaching the age of 7 years. Tables of mortality are given showing death rates in the cohort at 1-yearly intervals. A peak of mortality (117 per 1,000) occurs between 9 and 14 months and a secondary peak (71 per 1,000) at 3½ years. The lowest mortality rate (nil per 1,000) is found at 51 years. It appears that the high mortality at 9 months is linked to the month of birth. Children born in the rainy season are more likely to die at age 9 to 14 months than children born in the dry season. The authors explain this by assuming that the children enter the first rainy season—a period of heavy infection, particularly with malaria-still under the umbrella of inherited immunity. By the time inherited immunity disappears they are ready to face the second wet season with a reserve of acquired immunity. The growth rate from birth up to the sixth month is parallel to that of British children, but there is a check in the second half of the first year of life. The Gambian children from 11 to 7 years remain lighter in weight and shorter than British children of the same age, although annual increments are the same in both groups.

The authors do not consider that malnutrition plays any great part in producing the high mortality. The change to adult-pattern food is gradual, kwashiorkor is rare, and the diet is not notably deficient in proteins or essential amino-acids. The cultivation of rice is carried

out entirely by women and this arduous task interferes with the care of children. The authors consider that this lack of maternal care, together with infectious diseases, are the most important factors contributing to the high infantile mortality and that malnutrition, while by no means absent, is more often secondary to disease than primary.

William Hughes

1356. Aldosterone Excretion in Acclimatization to Heat K. A. FLETCHER, C. S. LEITHEAD, T. DEEGAN, M. A. PALLISTER, A. R. LIND, and B. G. MAEGRAITH. Annals of Tropical Medicine and Parasitology [Ann. trop. Med. Parasit.] 55, 498-504, Dec., 1961 [received Feb., 1962]. 2 figs., 9 refs.

It has been suggested that the adrenocortical steroids, by responding to the need for conservation of body salt, play an important part in man's acclimatization to heat. In this study, reported from the School of Tropical Medicine, Liverpool, urinary aldosterone excretion was measured in consecutive 24-hour volumes of urine collected from 9 healthy young men for 3 days before their departure from the United Kingdom and for 5 days after their arrival in Kuwait during the period of extreme summer heat there. Similar measurements were made in 5 comparable subjects resident in the United Kingdom and in 8 U.K. subjects resident in Kuwait.

The range of aldosterone excretion in 32 24-hour specimens of urine collected in the United Kingdom from 14 of the subjects was 1.8 to 19.2 µg. per 24 hours, with a mean of $8.7\pm3.7 \,\mu g$. No significant changes in aldosterone excretion were noted in the 6 subjects who performed only light duties on arrival in Kuwait, but there was a significant increase in the urinary aldosterone excretion over control values $(15.2\pm7.5 \mu g.$ compared with $7.7\pm4.1 \mu g$. per 24 hours) in the 3 subjects who began work on the day of arrival in Kuwait and limited their water intake and took no extra salt. For the 8 long-standing British residents in Kuwait the aldosterone values ranged from 5.0 to 25.0 µg, with a mean of 13.4 ± 6.8 µg. per 24 hours. The values for urinary volume and urinary chloride excretion are also reported. It is concluded that the results obtained in this study neither prove nor disprove the suggestion that the adrenal cortex plays a leading role in acclimatization to heat. R. R. Willcox

1357. Role of Nutritional Deficiencies in Tropical Sprue T. L. Althausen, L. C. Demelendez, and E. Pérez-Santiago. American Journal of Clinical Nutrition [Amer. J. clin. Nutr.] 10, 3-10, Jan., 1962. 22 refs.

The authors, working at the U.S. Army Tropical Research Medical Laboratory, Puerto Rico, have studied dietary deficiencies in 86 patients, 50 male and 36 female, with sprue, a group of 10 women with megaloblastic anaemia of pregnancy being also investigated for com-

parison. A dietary history covering several years was obtained in each case and from this the content in terms of calories, protein, vitamins A and C and those of the B complex, and calcium and iron was calculated, these values being then compared with the optimum and minimum standards recommended by the (U.S.) National Research Council.

By the latter criteria it was found that vegetable content was deficient in 87% of patients with sprue and 100% of those with anaemia of pregnancy, the comparable figures for deficiency of meat content being 61 and 60% respectively. Altogether 21% of the sprue patients showed dietary deficiencies of all the principal foodstuffs. Their intake of calcium and thiamine was adequate, but there was moderate deficiency in calories, protein, and riboflavine and severe deficiency of niacin and vitamins A and C. Comparison of the diets of the · female patients with sprue and of those with anaemia of pregnancy showed that in both groups the intake of protein and calcium, was similar, but that the intake of the anaemic patients was lower in respect of all other ingredients. Before treatment the serum albumin-level in the sprue group averaged 3.9 g. per 100 ml. and the globulin level 2.7 g. per 100 ml.; after treatment they rose to 4.4 and 2.9 g. per 100 ml. respectively, that is, to within the normal range for Puerto Ricans. This recovery occurred after treatment with antibiotics, although the diet was purposely maintained more deficient than the diet on which sprue occurred.

The authors state that sprue occurs mostly in the lower-income groups and note that there has recently been a marked reduction in its incidence which has run parallel with a rise in the general standard of living in Puerto Rico. Folic acid or vitamin B12 is an efficient palliative treatment of sprue. Against these facts in favour of a dietary deficiency as the cause of sprue are the findings that it does occur occasionally in wellnourished Puerto Ricans in the higher income groups and also in U.S. Army personnel stationed in Puerto Rico. One case is quoted in which a serviceman developed sprue while in Puerto Rico, recovered without treatment on his being transferred to the U.S. Middle West, but relapsed again when he returned to Puerto Rico. There is also the finding that sprue does not occur among negro subjects in Puerto Rico. These observations, together , with the finding that the diet was more deficient in patients with anaemia of pregnancy than in those with sprue, suggest that nutritional deficiency alone cannot account for the actiology and symptoms of sprue, and the authors suggest that there is a genetic factor as well which impairs intestinal absorption, concluding that it is in circumstances in which both factors operate that · William Hughes sprue occurs.

1358. The Treatment of Schistosomlasis with TWSb/6 D. M. FORSYTH. Annals of Tropical Medicine and Parasitology [Ann. trop. Med. Parasit.] 55, 407-409, Dec., 1961 [received Feb., 1962]. 17 refs.

At Southwell Hospital, Kuwait, 23 previously untreated Arab patients with schistosomiasis, 10 infected with Schistosoma mansoni and 13 with S. haematobium,

were treated with antimony dimercaptosuccinate (TWSb/6). As the standard preparation caused considerable local pain 2 g. of the salt was dissolved in 8 ml. of sterile normal saline to which was added 2 ml. of 2% procaine hydrochloride. Daily intramuscular injections of 2 ml. were given for 5 days, half an hour after the previous administration of 0.2 g. of amylobarbitone sodium and two compound tablets of codeine. Few of the patients complained of local pain with this regimen, although some pain was experienced by 13 of them; nausea and anorexia were other side-effects. Of 18 patients tested 16 developed electrocardiographic changes believed to have been due to the antimony.

One boy developed fever on the third day of treatment and the drug was discontinued; he was later found to be suffering from pulmonary tuberculosis and was excluded from the series. Of the remaining 22 patients 7 with S. mansoni and 8 with S. haematobium infection were cured, 4 patients were lost to follow-up, 2 refused to complete the course, and one continued to pass viable ova of S. haematobium. Although the drug has the advantage that it can be given intramuscularly it appears to be at least as toxic as other antimonials and is not considered suitable for the treatment of ambulatory outpatients!

R. R. Willcox

1359. Effects of Bilharziasis on Development of Egyptian Children

M. NABAWY, M. GABR, and M. M. RAGAB. Journal of Tropical Medicine and Hygtene [J. trop. Med. Hyg.] 64, 271–277, Nov., 1961. 5 figs., 9 refs.

Examination of urine from 918 and stools from 839 out of 1,000 children attending the out-patient clinic at the Munira Children's Hospital, Cairo, for different ailments showed that 104 boys and 28 girls had active bilharziasis.

For an analysis of the effects of this infection on physical development patients with a haemoglobin value of less than 65% and those with a history of malnutrition and other diseases were excluded. Most were urinary infections due to Schlstosoma haematoblum, though these ova were also found in the stools in 18 cases, while in 23 others the ova of S. mansoni were found in the stools in 18% of the infected children the height measurement was below the 10th percentile and 18.6% had radiographic evidence of delayed skeletal maturation. Genital hypoplasia was also noticed in a few males.

Clement C. Chesterman

1360. A Trial of Banocide as a Means of Controlling the Transmission of Loiasis on a Rubber Estate in Nigeria B. O. L. Duke and P. J. Moore. Annals of Tropical Medicine and Parasitology [Ann. trop. Med. Parasit.] 55, 263–277, Oct., 1961. 4 figs., 6 refs.

This trial of diethylcarbamazine citrate ("banocide") as a microfilarial suppressant was carried out at Sapele, Western Nigeria, on a rubber estate, this being considered a suitable place for such a trial because of the presence of a well-disciplined labour force working near a swampy forest, a breeding ground of the *Chrysops* fly, the intermediate host. The populations of neighbouring villages

were also included in the trial. A pre-treatment blood survey was carried out, and 444 carriers of *Loa* microfilariae were detected-among an estimated total population at risk of 5,120. Of these carriers, 427 were given a course of diethylcarbamazine citrate, the dosage for adults being 200 mg. three times daily for 20 days and for children proportionally less. One month later a first post-treatment blood examination was carried out, when 506 blood films were examined. Altogether, out of a total of 3,539 persons whose blood films were examined in the pre-treatment survey, 455 were found to be carriers of *Loa* microfilariae and given treatment with diethylcarbamazine citrate.

Six months later a second post-treatment examination was carried out on as many of the original positive subjects as could be found, only 272 blood films being obtained on this occasion. All patients treated were warned of the possibility of a reaction and the first tablet was swallowed in the presence of the medical officer. Such reactions were common, but not severe enough to warrant discontinuation of drug therapy. The authors believe that the majority of the subjects completed the course of diethylcarbamazine citrate. After the first course no attempt was made to give further treatment. to the villagers, although the rubber estate workers and their families were given a single tablet, 200 mg, for adults and 50 mg, for children, monthly on pay-day in order to keep down their microfilarial counts during the period of the trial.

Results were assessed by noting the effect of treatment on the infection potential of the human population as judged by the numbers of Loa microfilariae in the peripheral blood, and also by assessing the Loa infection rate in Chrysops silacea and Chrysops dimidiata in the district. Since only about 80% of the estate workers and just over 60% of the villagers cooperated in the trial the authors, in calculating their results, assumed that the unexamined portion of the population would contain the same proportion of infected persons as was found in the sample examined and that their infections would be of a similar intensity. The results were judged to be highly successful in that among the villagers the infection potential was reduced to between 6 and 12% of the pre-treatment level, and in the estate workers the infection potential was maintained at 2 to 4% of that level. Over the whole population at risk the estimated infection potential was reduced to some 30% of the pre-treatment figure. The results of the campaign, as judged by the effect on the transmission of Loa by C. silacea, showed a reduction to about 50% of the pre-treatment level. This reduction was less than that seen in the infection potential of the population at risk and suggests that although the majority of infections in C. silacea were derived from human beings in the area of the trial, a number of them probably originated from human sources outside the control area. No reduction was observed in the infection rate of the C. dimidiata population during the season of following treatment. The authors suggest that this may be due to some infections in this species being acquired from non-human hosts, or possibly because this fly has long flight range and may obtain its blood meals over a larger area than that covered by the trial. (A third

suggested possibility is observer error among the technicians who examined the dissected flies.) Although the trial was initially promising—in theory at least—the authors conclude that the method is unlikely to be of much practical importance in controlling the transmission of loiasis.

P. T. Main

1361. Comparative Trial of Drugs in Bacillary Dysentery S. W. Bible, K. Balasubramaniam, M. P. M. Cooray, and J. Gulasekaram. Journal of Tropical Medicine and Hygiene [J. trop. Med. Hyg.] 64, 300-302, Dec., 1962. 11 refs.

This clinical trial was carried out at Angoda Fever Hospital, Colombo, Cevlon, to compare the efficacy of four drugs in the treatment of bacillary dysentery due predominantly to Shigella flexneri. Patients were included in the trial only if they had received no previous treatment, were passing three or more unformed stools with blood and mucus daily, were suffering from tenesmus, and had stools which were compatible both macroscopically and microscopically with bacillary, and not amoebic, dysentery. The organisms were identified after stool cultures by their non-motility, biochemical reactions, and slide agglutination with specific antisera. Each patient was allocated in a random fashion to one of four treatment groups, each of 20 patients, which were treated as follows: (1) sulphadimidine, 2 g. initially. followed by 1 g. six-hourly for 5 days; (2) sulphamethoxypyridazine, 1 g. on the first day and 0.5 g. daily for a further 4 days; (3) the proprietary preparation "streptotriad" (consisting of 65 mg. of streptomycin sulphate; 65 mg. of sulphamerazine, 100 mg. of sulphadiazine, and 100 mg. of sulphathiazole, in each tablet), 3 tablets being taken three times daily for 5 days; and (4) tetracycline, 250 mg. six-hourly for 5 days. Symptomatic freatment and diet were the same for all groups. Treatment was concluded on the 5th day and a stool and rectal swab were examined on the 3 following days, the patient being considered bacteriologically cured if specimens on all 3 days were negative.

On clinical grounds tetracycline was judged to give the best results, but the difference between any two forms of treatment was not statistically significant. When bacteriological cure was considered, however, tetracycline was found to be significantly superior to the other three forms of treatment; while these latter showed no statistical difference in regard to efficacy as between themselves. There were no side-effects with any of the four drugs administered during the trial. Tetracycline cured the 6 patients in whom the other forms of therapy had failed.

The authors conclude that in the treatment of bacillary dysentery, commonly due to Sh. flexneri, the combination of streptomycin with a sulphonamide is unnecessary, since sulphonamides alone would give the same results. They suggest that a practical approach would be to begin treatment with a long-acting sulphonamide and if this failed to turn to tetracycline to bring about clinical and bacteriological cure; the great disadvantage of tetracycline is its high cost.

P. T. Main

Allergy

1362. Influenza Virus Sensitisation in Bronchial Asthma: a Study of Bronchial Provocation Tests with Influenza Virus and Bacterial Extracts. [In English]

M. K. HAJOS. Acta allergologica [Acta allerg. (Kbh.)] 16, 347-363, 1961. 8 figs., 10 refs.

The author of this paper from the State Institute of Rheumatology and Medical Hydrology, Budapest, states that observations made during the Asiatic influenza pandemic in 1957 suggested that influenza viruses as well as bacteria might be important causes of asthma. Direct bronchial provocation tests were used to determine the significance of influenzal sensitization. In 262 patients with infective bronchial asthma skin and bronchial tests were carried out with extracts of bacterial and viral cultures. The results of bronchial tests showed a better correlation with influenzal history than did the results of skin tests alone. Reactions to influenza virus were often associated with reactions to Haemophilus influenzae. It is suggested that specific desensitization with vaccines plays an important part in the management of asthma in children and young adults. A. W. Frankland

1363. Anti-asthmatic Effect of Phenazone and Amidopyrine

H. Herxheimer and E. Stresemann. Nature [Nature (Lond.)] 192, 1089–1090, Dec. 16, 1961. 2 figs., 6 refs.

The anti-asthmatic effects of phenazone and amidopyrine were studied in patients at the Rudolf Virchow-Krankenhaus, Berlin. For this purpose 27 patients received phenazone in doses of 0.5, 1, or 2 g. in 63 experiments and 26 received amidopyrine in doses of 0.6, 1.2, 1.5, or 1.8 g. in 43 experiments. A placebo was given in 17 experiments. In the majority of cases there was an improvement in the vital capacity with both drugs, but the placebo had no appreciable effect. The forced expiratory volume was determined before and after administration of the drugs but no definite effect was observed; however, the peak flow was usually increased when the vital capacity increased. It is suggested that the anti-asthmatic action of these drugs may be due to inhibition of histamine release or to specific antagonistic effect to bradykinin. Further work on the relationship between bradykinin and asthma is being carried out.

R. S. Bruce Pearson

1364. Experimental Eosinophilia: Local Tissue Reaction to Ascaris Extracts

J. VAUGHN. Journal of Allergy [J. Allergy] 32, 501-513, Nov.-Dec., 1961. 4 figs., 24 refs.

In this study of experimental eosinophilia carried out at Baylor University College of Medicine, Houston, Texas, guinea-pigs were given 2 subcutaneous implants of either 0.25 mg. of Ascaris polysaccharide or 25 mg. of insoluble Ascaris protein. In both cases one skin wound was sealed and the other left unsealed; the animals were killed at intervals of 3 to 72 hours. The

polysaccharide was found to cause a brisk eosinophilia but a minimal response in the tissues. The blood changes after implantation of protein were small and erratic, but there was a marked tissue reaction of the foreign-body granuloma type in which numerous eosinophils were present.

H. Herxhelmer

1365. Studies with Dust Extracts

H. E. PRINCE, T. S. PAINTER JR., M. B. MORROW, and G. H. MEYER. *Annals of Allergy [Ann. Allergy]* 19, 1389–1398, Dec., 1961. 1 fig., 6 refs.

This is the report of a collaborative study of "the allergenicity of dusts from various environments for patients sensitive to house dust", carried out by physicians from 17 States of the U.S.A. Vacuum-cleaner dust was collected from the houses of dust-sensitive asthmatic subjects and from hotels, dormitories, a doctor's consulting-room, and a department store; feather-pillow dust was also collected. Extracts of the dust were dialysed and acetone-precipitated and used for comparative skin testing of dust-sensitive patients. It was found that the dust from patients' houses was more antigenic than all the other dusts, including feather-pillow dust, with the exception of that from one dormitory. The geographic area from which the dust came made no difference to the results. Microscopical investigation of the house dusts gave uniform results, with frequent occurrence of mould spores, insect and plant debris, animal hairs, and tissue fibres. H. Herxheimer

1366. Purification and Properties of House Dust Allergen. [In English]

L. Berrens and E. Young. International Archives of Allergy and Applied Immunology [Int. Arch. Allergy] 19, 341-359, 1961. 3 figs., 13 refs.

The object of the investigation described in this paper from the Academic Hospital, State University, Utrecht, was twofold-to isolate from crude house dust a fraction with a high skin-reacting activity and at the same time to study the nature of the contaminants. Benzoic-acid precipitation, 25% ammonium sulphate, and then saturated ammonium sulphate were used in fractionation and purification procedures. Six different fractions were prepared and the protein nitrogen, amino-acid, and carbohydrate contents of each were determined. Skin tests were performed on known dust-sensitive patients on a quantitative basis and also on patients without symptoms of house-dust allergy who did not react to two commercial house-dust extracts. It was found that the extracts were contaminated with a relatively large amount of unreactive acid polysaccharides and with human dandruff allergens. The house-dust allergen is very specific and can be isolated with a high degree of purification with a molecular weight of 22,000 to 25,000. It contains 7.% protein nitrogen and 44% hexose. It is a mucoprotein of probable plant origin. A. W. Frankland

Nutrition and Metabolism

1367. Change of Diet of Yemenite Jews in Relation to Diabetes and Ischaemic Heart-Disease

A. M. COHEN, S. BAVLY, and R. POZNANSKI. Lancet [Lancet] 2, 1399-1401, Dec. 23, 1961. 24 refs.

Various previous investigations have indicated that the change of diet of Yemenite Jews after settlement in Israel leads to a greater prevalence of diabetes, ischaemic heart disease, and hypertension and to increased plasma cholesterol and β -lipoprotein levels. In the study here reported from Hadassah University Hospital and the College of Nutrition and Home Economics, Jerusalem, 20 Yemenite families who had lived in Israel for less than 10 years were surveyed and their diet in the Yemen determined by the "recollection" method; the diet of another 20 Yemenite families who had lived in Israel for longer than 25 years was determined for comparison. In this survey a dietitian trained in Israel was employed who had arrived only 10 years earlier from Yemen and was familiar both with the way of living in the old country and with the habits of the immigrants.

It was found that apart from a slight increase in the total calorie intake, which was reflected in an increase in the body weight, the total protein, fat, and carbohydrate intake was practically the same in both groups. The authors state that in Yemen most of the fat used is of animal origin, and that Yemenites in Israel consume far more oil (sesame, soya, and olive) than the Yemenites in Yemen. While the total carbohydrate intake was very similar in both groups, up to 5 or 6 times more refined sugar is eaten by Yemenite settlers in Israel than is available in Yemen.

The authors submit that "if nutrient is an aetiological factor in ischaemic heart-disease or diabetes, the increased consumption of sucrose might be responsible, directly or indirectly, for the higher prevalence of these diseases in those Yemenites who have lived for many years in Israel". [Some of the facts given and conclusions reached in this paper are in sharp contrast with the findings of previous investigations.]

Z. A. Lettner

1368. Effect of Thyroxine Analogue TFA-4 on Serum Cholesterol

V. L. Love. Archives of Internal Medicine [Arch. intern. Med.] 108, 833-836, Dec., 1961. 3 figs., 9 refs.

To 18 men and 11 women (mean ages 51.7 and 55 years respectively) suffering from coronary arterial disease tetraiodothyroformic acid (TFA-4) was given, after 4 to 6 weeks of placebo treatment, in doses of 100 to 200 mg. three times a day. The patients were examined monthly for 9 to 10 months and the diet, which in 20 cases had been low in cholesterol and animal fat content, remained unchanged throughout the study.

The serum cholesterol level was substantially lowered in 20 patients (in 9 patients by over 100 mg. per 100 ml. and in 11 by more than 50 mg. per 100 ml.); in 6 patients the reduction was less than 50 mg. per 100 ml. and in

the remaining 3 cases no reduction in level was achieved. The maximum reduction in the serum cholesterol level occurred after 5 to 6 months' administration of TFA-4 and this lowered level was maintained for several months afterwards. No patients in this series showed any increase in the anginal symptoms or suffered any episode of cardiac infarction during the administration of TFA-4. However, 5 patients developed acneiform skin eruptions on the face, neck, and chest, which was probably due to the iodine content of the drug, while 5 (including 2 of those with the skin rash) experienced an "irritable colon syndrome" manifested by 2 to 4 explosive bowel movements in the morning.

[Thyroxine analogues are interesting substances for the reduction of the serum cholesterol level, but all such compounds so far tried have caused unpleasant side-effects which often necessitate the interruption of their administration.]

Z. A. Leitner

1369. Plasma-lipids in an African Tribe Living on a Diet of Milk and Meat

A. G. Shaper, M. Jones, and J. Kyobe. *Lancet* [Lancet] 2, 1324–1327, Dec. 16, 1961. 33 refs.

At Makerere College Medical School, Uganda, the authors have investigated the plasma lipid levels in 102 "warriors" (mean age 26 years) and 99 "elders" (mean age 46 years) of the Samburu tribe, a nomadic tribe of Northern Kenya living mainly on milk, supplemented occasionally with meat. Milk consumption of an active adult ranged from 2 to 10 litres per day depending on the season. The average fat content of the milk was 5.6 g. per 100 ml. and provided some 60% of the total caloric intake of about 5,000 Cal. daily. The various plasma lipid levels (in mg. per 100 ml.) were: cholesterol 166, phospholipids 212, total fatty acids 254, triglycerides 85. These concentrations are similar to those found in Africans living on a low-fat diet. M. Lubran

1370. The ¹³¹I-Triolein Fat-absorption Test W. S. REITH, E. S. WILLIAMS, and M. J. THOMAS. Lancet [Lancet] 2, 1229–1232, Dec. 2, 1961. 2 figs., 20 refs.

In the studies of fat absorption here-reported from the Middlesex Hospital Medical School, London, a test meal consisting of 5 to 50 μ c. of ¹³¹I-labelled triolein in 15 ml. of olive oil and 120 ml. of skimmed milk, homogenized mechanically without use of "emulsifying agents", was given on 81 occasions to 65 subjects, of whom 34 were thought to have defective absorption or utilization of fats. Blood was taken 2, 3, 4, and 6 hours after the meal and the whole-blood radioactivity determined as a percentage of the dose, using a height-weight nomogram to calculate the blood volume. The area bounded by the blood activity curve, the abscissa, and the 6-hour ordinate was cut out and weighed, and expressed as a percentage of a similar area (derived from 8 normal subjects) bounded by the mean normal value

plus one standard deviation, the resulting percentage being termed the "relative manipulation curve area" (R.M.C.A.).

Abnormally low R.M.C.A. values were found in most patients with steatorrhoea whether this was idiopathic, followed partial gastrectomy or pancreatectomy, or was due to Crohn's disease or lipid storage disease. Low values were also found in non-steatorrhoeic patients suffering from malignant neoplasm or from depression and anxiety, while some abnormal results were also obtained in patients with Hodgkin's disease. The test gave satisfactory reproducible results and these also correlated well with the clinical assessment based on the history, laboratory tests, and therapeutic response. It is suggested that previous unreliable results with the labelled triolein test may have been due in part to the unphysiological nature of the test meal employed.

M. Lubran

1371. The Action of Chorionic Gonadotrophin in the Obese

S. CARNE. Lancet [Lancet] 2, 1282-1284, Dec. 9, 1961.

In a double-blind trial of the effect of chorionic gonadotrophin in the obese two groups of such subjects were maintained on a 500-Calorie diet for 6 weeks, and the weight loss in one group receiving daily injections of chorionic gonadotrophin was compared with that in the group given daily injections of saline. The dosage of chorionic gonadotrophin ("antuitrin S") was 0.25 ml. daily for 6 days each week. The patients who received chorionic gonadotrophin lost slightly more weight than those given a daily injection of saline, but the difference was not significant at the 5% level.

In a second trial patients who were weighed daily and given injections of saline each day lost significantly more weight than those who were weighed only twice a week and given no injections. The author concluded that patients who were weighed daily under supervision seemed to find it easier to adhere to a strict diet than those who were weighed less frequently, and that weight loss was most satisfactory in those patients joining a "group session", which provided an opportunity to "compare notes".

A. G. Mullins

1372. Copper Metabolism in Wilson's Disease, Laennec's Cirrhosis and Hemachromatosis: Studies with Radiocopper (Cu⁶⁴)

W. J. MAYTUM, N. P. GOLDSTEIN, W. F. McGUCKIN, and C. A. OWEN JR. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 36, 641–660, Dec. 6, 1961. 13 figs., 49 refs.

The error in copper metabolism which results in Wilson's disease (hepatolenticular degeneration) has recently been studied by various authors by the use of radioactive copper (64Cu) and certain basic steps have been clarified. In the present study, carried out at the Mayo Clinic, 64Cu was used in order to establish as many differences as possible between 5 patients with Wilson's disease, 2 with other hepatic disease (Laënnec's cirrhosis), 2 with haemochromatosis, and 7 healthy adults. The 64Cu, which has a half-life of 12.8 hours, was adminis-

tered intravenously in doses up to 1,700 μ c. and containing 72 to 12,500 μ g. of copper; in addition, 2 of the patients with Wilson's disease and 4 of the controls received 64Cu orally. The radioactivity in the plasma, urine, and faeces was measured during the study period of 3 to 4 days, and counts were made *in vivo* over the liver, calf, kidneys, and head. The plasma protein-bound 64Cu level was determined by "salting out", that is, separating the albumin-bound from the globulin-bound copper by means of a saturated solution of ammonium sulphate, and also by starch electrophoresis.

The radioactivity induced in the plasma by an intravenous injection of 64Cu showed an initial rapid fall inall subjects, but this was soon followed by a rising level in all subjects except the patients with Wilson's disease. Analyses of the plasma by "salting out" and by electrophoresis showed an almost complete lack of ceruloplasmin-bound 64Cu in the patients with Wilson's disease. as contrasted with a rising level in the remaining patients, the distinction being clear from the 6th hour and most conspicuous at 24 hours after the intravenous dose. The patients with Wilson's disease excreted relatively large amounts of copper in the urine following its oral or intravenous administration, whereas in the remaining subjects such excretion was only small. The counts in vivo showed that in Wilson's disease the uptake of 64Cu by the liver was slower and less in amount and its release. more retarded than in the normal subjects; the patients with other hepatic disease showed some defect of uptake or release by the liver, but the abnormality was much less than that in Wilson's disease. Radioactivity over the calf was at least twice as high in patients with Wilson's disease. A large transfusion of plasma in one patient with Wilson's disease failed to alter the distribution of radioactive copper. Joseph Parness

1373. The Intestinal Absorption Defect in Cystinuria M. D. Milne, A. A. M. Asatoor, K. D. G. Edwards, and L. W. Loughridge. *Gut* [*Gut*] 2, 323–337, Dec., 1961. 11 figs., bibliography.

In this study of cystinuria carried out at the Postgraduate Medical School of London lysine and ornithine hydrochlorides were fed to homozygous cystinuric patients and to normal control subjects. In the cystinurics it was found that a considerable fraction of the aminoacids appeared unchanged in the faeces, indicating incomplete absorption. In the normal subjects, however, absorption was complete, except in 3 individuals who had "intestinal hurry" with watery diarrhoea. The cystinuric patients showed an increased faecal output of arginine after the ingestion of lysine and ornithine, but this did not occur in the normal controls, suggesting that in cystinuric patients there is saturation of a common intestinal transport system.

It is concluded that cystinuria and Hartrup disease are closely related conditions and that the results of the present study indicate that the defect in amino-acid transport known to occur in the renal tubules of cystinurics is also present in the gut. The results of studies of the excretion of cadaverine, putrescine, and the heterocyclic amines piperidine and pyrrolidine were consistent with this view.

H. Harris

Gastroenterology

1374. The Functional Anatomy of the Lower Third of the Oesophagus and Its Significance for the Diagnosis of Sliding Hiatus Hernia. (Zur funktionellen Anatomie des unteren Ösophagusdrittels, Ihre Bedeutung für die Diagnostik sogenannter Gleithernien) –

E. BUCHHEIM and H.-J. MAURER. Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin [Fortschr. Röntgenstr.] 95, 624-633, Nov., 1961. 8 figs., bibliography.

The authors assume that below the thoracic oesophagus there is a special gastro-oesophageal vestibule which is partly above and partly below the diaphragmatic level. This vestibule differs in function from the rest of the oesophagus. They have studied the behaviour of the vestibule with the aid of serial films taken with the "rapidix" cassette and an "odelca" camera, considering that this method is superior to cinematography and exposes the patient to less radiation. They discuss the radiological appearances of the normal vestibule and of various types of sliding hernia.

F. M. Abeles

1375: Treatment with Ribonucleic Acids in Liver Disease. (La thérapeutique par les acides ribonucléiques dans les maladies du foie)

M. Cachin, F. Pergola, J. de Brux, and P. Brun. Presse médicale [Presse méd.] 69, 2612-2614, Dec. 25, 1961. 8 figs., 2 refs.

On the basis of the observation that the amount of intracellular nucleic acids is reduced in patients with acute or chronic hepatitis, the authors have given daily intramuscular injections of an extract of animal pancreas rich in ribonucleic acids for 2 weeks to 26 patients with liver disease. A battery of biochemical tests of liver function were performed before and after treatment, and in 14 cases specimens of liver for histological examination were also obtained by needle biopsy.

In 8 patients with viral hepatitis clinical and biochemical improvement was found to be prompt. In 4 malnourished alcoholic patients with fatty liver there was clinical and biochemical improvement with considerable reduction in the amount of intracellular fat, together with histological evidence of increased intracellular nucleic acid content. In 14 patients with alcoholic cirrhosis or "pre-cirrhosis" with varying clinical manifestations clinical improvement occurred, although biochemical improvement was less definite; of 10 of these patients 7 were thought to show an increase in intracellular nucleic acids.

[These observations were uncontrolled and, as the authors themselves admit, rest, withdrawal of alcohol, administration of antibiotics, and a suitable hospital diet can produce striking improvement in such patients, in whom the reduction in the amount of liver fat can often be astonishing.]

P. C. Reynell

1376. The Pathogenetic Therapy of Acute Pancreatitis. (Патогенетическая терапая острого панкреатита) G. M. Nikolaev. Советская Медицина [Sovetsk. Med.] 25, 21–25, Dec., 1961. 37 refs.

The author has treated "pathogenetically" 16 cases of acute oedema of the pancreas and describes a typical case occurring in a woman aged 57 who presented with abdominal pains and severe sickness. Examination showed the abdomen to be distended, but not rigid, and to give a positive Mayo-Robson sign. The quantity of diastase in the urine was 256 units. A diagnosis of acute pancreatitis was made. After a bilateral blockade of the abdominal nerves and the sympathetic stems with procaine the pains disappeared and the patient rapidly recovered.

The reasons for this quick amelioration of the condition are said to be (1) the powerful anti-shock action of the blockade; (2) increased intensity of phagocytosis; (3) diminution of the secretion of pancreatic juice; (4) abolition of the spasm of Oddi's sphincter; (5) reduction in the degree of intoxication; and (6) return of the tonus of the gastro-intestinal tract to normal. The author recommends bilateral procaine blockade in all acute cases of pancreatitis, the main contraindications being decompensated heart disease and emphysema of the lungs or pneumosclerosis. There must be no doubt about the diagnosis of pancreatitis. He states that acute oedema of the pancreas occurs in some 75 to 80% of all cases of pancreatitis.

STOMACH AND DUODENUM

1377. Civilisation and Peptic Ulcer M. Susser and Z. Stein. Lancet [Lancet] 1, 115-119, Jan. 20, 1962. 3 figs., 23 refs.

This paper from the University of Manchester suggests that factors operating in the last quarter of the 19th century may have exerted an influence on persons born during that period which increased the incidence of peptic ulcer among them—an added liability to ulcer which this generation has carried throughout adult life. This suggestion is based on cohort studies of ulcer mortality and sickness rates during successive decades from 1920 to 1959. From the figures given it would appear that deaths from peptic ulcer in England and Wales reached a peak in the 1950's, and have since begun to decline.

The authors discuss possible causes for this fluctuation in death rates, which is also apparent in sickness rates. They do not believe that uneven distribution of treatment is the cause, even though both surgical and medical treatments—for example, partial gastrectomy and fuller dietary regimen—have markedly changed since the early and middle 1930's. Their conclusions are drawn from a

consideration of figures for perforations and returns from the Registrar-General's department, and from a number of papers, most of which have been published in Great Britain. It is thought that the decline in duodenal ulceration is occurring about 5 years later than that in gastric ulceration, and that the recession in the incidence of duodenal ulcer is most evident among men in the higher social classes. It is concluded that duodenal ulcer is not a disease of civilization in the sense of the stresses of an industrialized society.

[Studies of "cohort" analysis type involve many variable factors, and it is not easy to draw final conclusions from those given in this interesting paper.]

Thomas Hunt

1378. The Use of a New Soviet Preparation—Fubromegan—in the Treatment of Peptic Ulcer. (Применение нового отечественного препарата фубромегана в лечении язвенной болевни)

T. S. MNACAKANOV, R. S. MAMIKONJAN, and A. M. TUMANJAN. *Клиническая Медицина [Klin. Med. (Mosk.)]* 39, 93–96, Nov., 1961. 8 refs.

"Fubromegan" (iodomethyl-α-methyl-γ-diethylaminopropyl-5-bromfuran-2-carbonate) is a ganglion-blocking substance with a strong cholinolytic action which was synthesized at the Armenian Soviet Institute of Organic Chemistry, Erevan. It is claimed to be of low toxicity and to have a wide range of action. The present authors have employed it in 48 cases of peptic ulcer with good results. The dosage was 10 mg. in a 2% solution given intramuscularly three times a day, increasing to 20 mg. four times daily for a period of 20 to 40 days. After 15 to 20 days' treatment 16 of the patients were able to change to oral therapy, the dosage being 0.15 to 3.0 g. daily. There were no side-effects beyond some dryness of the mouth, which soon passed off. Of the 48 patients 14 had gastric and 34 duodenal ulcer. In 31 cases the symptoms were under 3 years' duration, but in the remainder had been present for 4 to 10 years. Haemorrhage had occurred in 5, 3 were suffering from mild pyloric stenosis, 18 had hyperchlorhydria, 7 had hypochlorhydria, and in 24 visible niches were seen on radiographic examination.

On the institution of treatment pain, heartburn, and vomiting rapidly disappeared, and later objective signs of healing were observed; in 16 of the hyperchlorhydric cases and in 6 of the hypochlorhydric cases the gastric acid secretion became normal, while in 13 of the 24 with niches these disappeared and in 8 they became much smaller. Those who did not respond were found to be suffering from meso-adenitis, chronic pancreatitis, or other complications. The longer course (40 days) was found to produce more lasting effect.

L. Firman-Edwards

1379. Early Diagnosis of Gastric Cancer

C. R. HITCHCOCK and S. L. SCHEINER. Surgery, Gynecology and Obstetrics [Surg. Gynec. Obstet.] 113, 665-672, Dec., 1961. 12 refs.

The authors have studied the problem of screening large numbers of apparently healthy people over 50 years old for cancer of the stomach. Among the first series of

12,000 patients seen at the Cancer Detection Center of the University of Minnesota Hospitals, Minneapolis, 77 patients with pernicious anaemia and 119 with a strong family history of cancer of the stomach were detected. The first group had an incidence of cancer of the stomach 21.3 times that of the "normal" population over 50; no cases of cancer of the stomach were found in the second group over a 7-year period. In the second series of over 9,000 patients the presence of pernicious anaemia. achlorhydria or hypochlorhydria (found in only 25% of subjects), a positive result for occult blood, and a strong family history of cancer of the stomach were used as indications for an annual barium-meal examination. The incidence of cancer of the stomach in patients with deficient gastric secretion was 3.2 times that of the "normal" population. However, the 5-year prognosis of cancer of the stomach detected by the Cancer Detection Center was as poor as that of cancer detected by other units. The authors consider that this might be related to the difficulty of detecting early cancer by barium-meal examination and suggest that the acridine orange technique for staining neoplastic cells in gastric aspirates might prove of value. They conclude that repeated screening of large numbers of people for cancer of the stomach does not usefully reduce the mortality.

· G. L. Asherson

1380. Aspirin and Gastric Bleeding: Further Studies of Calcium Aspirin

A. Muir and I. A. Cossar. American Journal of Digestive Diseases [Amer. J. dig. Dis.] 6, 1115–1125, Dec., 1961. 2 figs., 36 refs.

This paper from Law Hospital, Carluke, Scotland, describes "blind" investigations of the possible detrimental effects of aspirin on gastric mucosa. To 197 patients two tablets (0.6 gramme) of standard aspirin or two tablets of soluble calcium aspirin in equivalent dosage were given in 100 ml. of water two hours before elective partial gastrectomy for duodenal ulceration. Multiple necrotic lesions, 2 to 5 mm. in diameter and containing drug particles, were found, usually on the lesser curve or posterior wall, in the resected specimens from 8 out of 102 patients who received standard aspirin; no notable lesions were seen in the specimens from 95 patients given soluble calcium aspirin.

In a second investigation two uncrushed tablets of either standard aspirin or soluble calcium aspirin were given with a little water to two groups, each of 30 dyspeptic patients, immediately after the withdrawal of fasting gastric juice. Specimens of gastric juice were examined for naked-eye evidence of haemorrhage every half-hour. Haemorrhage occurred in just over half the patients in each group. However, in a further investigation in 20 patients without a history of dyspepsia, soluble calcium aspirin produced significantly less gastric bleeding (5%) than did standard aspirin (65%)

A. Wynn Williams

1381. Mechanisms Protecting against Gastro-oesophageal Reflux: a Review

M. ATKINSON. Gut [Gut] 3, 1–15, March, 1962. 7 figs., bilbiography.

Cardiovascular System

1382. Primary Pulmonary Hypertension: with Special Reference to Prognosis. [In English]

N. C. NIELSEN and J. FABRICIUS. Acta medica Scandinavica [Acta med. scand.] 170, 731-741, Dec., 1961. 5 figs., 20 refs.

Out of 6,000 patients examined at the cardiological department of Rigshospitalet, Copenhagen, between - 1947 and 1960, a diagnosis of primary pulmonary hypertension was made in 14 cases by means of cardiac catheterization. Of these patients, 6 male and 8 female, 10 have died and necropsy was performed on 4 of them. The ages ranged from 8 to 50 years. In 8 cases the pulmonary arterial pressure was over 70 mm. Hg and these patients fared less well than the others, right heart failure developing early. In 6 cases in which the pressure in the pulmonary artery was measured during exercise (raising the legs) the pressure rose. All patients had symptoms of breathlessness on exertion, and in 10 there was exertional syncope, 6 had angina of effort, 5 showed cyanosis, but in no case were there any marked abnormal lung signs. In 10 a systolic murmur was present which was best heard in the pulmonary area, while the pulmonary second sound was increased in all but one.

In 10 of 12 cases in which electrocardiography was carried out it showed an R wave in Lead V1 greater than the S wave and in the severe cases the T wave was inverted in Leads V1 to 5. Radiology in 12 cases revealed an enlarged pulmonary conus, and enlargement of the heart in 9. Treatment for the heart failure was along conventional lines; amyl nitrite proved of some value for exertional syncope. In the cases coming to necropsy the post-mortem findings included hypertrophy of the right atrium and ventricle, the smaller branches of the pulmonary artery showing hypertrophy of the media together with subintimal fibrosis. The clinical course of the disease is unpredictable, but of 5 patients subjected to serial cardiac catheterization over the course of 3 to 6 years the pulmonary arterial pressure rose in 2 and remained unchanged in 3. The prognosis, in terms of life expectancy, varied from a few months to 20 years.

, G. S. Crockett

1383. Effects of Controlled Acute Hemorrhage on Myocardial Contractlle Force

L. Greenfield, P. A. Ebert, and W. G. Austen. Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol. (N,Y.)] 107, 858-861, Aug.-Sept. [received Nov.], 1961. 3 figs., 12 refs.

The role of myocardial changes in the causation of death following acute haemorrhagic shock is still a matter of debate. In this experimental study, reported from the National Heart Institute, Bethesda, Maryland, the authors measured the myocardial contractile force during haemorrhage in 20 dogs in order to assess the onset and extent of myocardial depression. The animals were

anaesthetized with thiopentone, and respiration main-tained through a cuffed endotracheal tube. One femoral artery was cannulated for recording the aortic pressure and the other connected to a reservoir to allow of controlled bleeding. Myocardial contractile force was measured by means of a strain gauge sutured across the anterior face of the right ventricle. Of the 20 dogs, 8 were bled at a rate which lowered the mean aortic pressure to 50 mm. Hg within 2 minutes, 8 were bled to this level in 5 minutes, another 4 to this level in 10 minutes, while the remaining 4 dogs were studied while undergoing total right heart by-pass.

With the onset of bleeding there was an initial increase in the heart rate and contractile force of the myocardium. but both decreased when the mean aortic pressure fell below 90 mm. Hg; the decrease in myocardial contractile force preceded slowing of the heart rate. The dogs subjected to total right heart by-pass responded in a similar way to a fall in blood pressure brought about by a reduction of the flow into the pulmonary artery. It is noted in the discussion that the constant relationship between. myocardial contractile force and arterial pressure and the simultaneous decrease in heart rate support the assumption that these changes are due to myocardial depression. One explanation might be that a mean arterial pressure of 90 mm. Hg represents a critical coronary perfusion pressure. The myocardial depression is thought to be probably metabolic in nature, but further experiments (to be published later) seemed to point also to some nervous influence. G. Clayton

1384. Myocardial Metabolism in Progressive Muscular Dystrophy

J. F. SUNDERMEYER, S. GUDBJARNASON, V. E. WENDT, P. B. DEN BAKKER, and R. J. BING. *Circulation [Circulation]* 24, 1348–1355, Dec., 1961. 3 figs., 40 refs.

Myocardial as well as skeletal muscle involvement occurs in a high proportion of cases of muscular dystrophy, constituting a specific cardiomyopathy. Clinically, this is manifested as a labile tachycardia, congestive heart failure, various arrhythmias and cardiac murmurs, cardiomegaly, and various electrocardiographic abnormalities. Pathologically, the myocardium shows similar changes to those found in skeletal muscle; subendocardial fibroelastosis may also occur.

The authors of this paper report an investigation into the cardiac metabolism of 11 patients with muscular dystrophy at Harper Hospital, Detroif, Michigan. Coronary blood flow was measured in 4 and cardiac output in 6 patients. The blood concentrations of oxygen, glucose, inorganic phosphate, pyruvate, and lactate and the serum activities of malic dehydrogenase and aldolase were determined in simultaneously drawn coronary sinus and arterial blood samples. The cardiac output was increased in all cases. From their findings

the authors suggest that anaerobic glycolysis occurs in the heart muscle. [For a discussion of the results the original paper should be consulted.]

R. Wyburn-Mason

1385. Treatment of Paroxysmal Atrial Arrhythmias with Acetyl-strophanthidin

J. Beregovich, R. Florenzano, and G. Dussallant. American Journal of Cardiology [Amer. J. Cardiol.] 8, 838-842, 4 figs., 13 refs.

This paper, coming from the Hospital del Salvador (University of Chile), Santiago, describes the results of the treatment with acetyl-strophanthidin of 10 episodes of arrhythmia (7 of supraventricular tachycardia and 3 of atrial flutter) in 9 patients who, with one exception, were all between 47 and 62 years of age. This drug is a synthetic derivative of strophanthin and produces effects similar to those of digitalis glycosides. It is given by slow intravenous injection (over 10 minutes) in doses of 0.25 to 0.5 mg. and produces its maximum effect within 5 to 10 minutes. The dose may be repeated after a 10minute interval, but the cumulative dosage should not exceed 1.0 mg. Its action lasts about 4 hours. In cases of serious cardiac impairment and those previously given digitalis medication it is wise to start with a reduced dose of 0.125 mg.

In most of the present patients symptoms had been prolonged or recurrent and had proved resistant to other forms of therapy. Treatment was carried out under careful clinical and electrocardiographic control. In 9 cases conversion to normal rhythm was obtained "with great promptness", and without any clinical or electrocardiographic signs of digitalis intoxication. Clinical details, together with electrocardiograms recorded during treatment, are given for 4 of the cases. The authors point out that the drug is potentially dangerous, but contend that slow administration permits a regulation of the dosage to within reasonably safe limits [a contention which seems justified by their own results].

Rex Matthews

1386. Cardiac Output and Blood Volume in Chronic Cor Pulmonale

C. R. Woolf, R. W. Gunton, and W. Paul. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 1271-1275, Dec. 9, 1961. 3 figs., 15 refs.

In an investigation at Toronto General Hospital cardiac output and blood volume were measured in 69 patients with lung disease, of whom 50 were emphysematous, 10 had diffuse pulmonary fibrosis, and 9 had kyphoscoliosis. Of the emphysematous patients, 12 were in right heart failure. For comparison, identical studies were performed on 6 patients with polycythaemia rubra vera and 73 control subjects without heart or lung disease. All subjects were examined clinically and radiologically and electrocardiograms were recorded. Forced vital capacity was measured with a spirometer, and maximum breathing capacity with a Douglas bag. As a test for emphysema, 90% desaturation time was measured by oximetry, which was also used to record changes in arterial oxygen saturation during a one-minute 30-step exercise test. Cardiac output and central blood volume

were determined from an ear-oximeter Evans blue (azovan) dye curve. Plasma and erythrocyte volumes were calculated from the plasma dye dilution and haematocrit.

Cardiac output was normal or low in 48 of the emphysematous patients; it was significantly lower in patients with heart failure. Output was raised in only one case each of kyphoscoliosis, pulmonary fibrosis, and polycythaemia rubra vera. The mean erythrocyte volume was significantly raised in those patients with emphysema or pulmonary fibrosis who had past or present right heart failure. Erythrocyte volume was also raised in polycythaemia, but not in the other groups. Plasma volume was normal in all groups.

This investigation confirms previous work which suggests that when blood volume is raised in chronic cor pulmonale the rise is almost entirely due to a raised erythrocyte volume.

D. Goldman

DIAGNOSTIC METHODS

1387. Observations on the Syndrome with Short P-Q Interval and Normal QRS Complex. [In English] M. REINIKAÏNEN. Annales medicinae internae Fenniae [Ann. Med. intern. Fenn.] 50, 149-161, 1961. 3 figs., 12 refs.

In a series of electrocardiograms (ECGs) of 15,900 patients examined at three medical clinics in Helsinki 52 were found in which the P-Q interval was 0.11 second or less, while the QRS interval was normal. These ECGs (Series 1) were compared with a control series from 52 patients without organic heart disease, in which the P-Q interval ranged from 0.13 to 0.18 second and the ORS complex was normal. In Series 1 the patients' ages ranged from 17 to 67 years, 24 being in the age group 20-40 years, and there was a preponderance (77%) of females. Of these patients 14 (27%) had a history of paroxysmal tachycardia compared with only 2 of the control series, but there was relatively little difference, in the incidence of premature beats-9 cases compared with 7 in the control series. The duration of the P-Q interval was: 0.11 second in 32 cases, 0.10 second in 18, 0.09 second in one, and 0.08 second in one. Neurosis was twice as common in Series 1 (17 patients, all female) as in the control series (8 cases). The mean duration of the ORS complex was 0.063 second and the mean P-J time was 0 168 second. In no case were ST-T changes seen. The conclusion reached is that "it is most likely that the syndrome with a short P-Q wave and a normal QRS complex is an entity, distinct from the WPW William A. R. Thomson syndrome ".

1388. The Krypton⁸⁵ Inhalation Test for the Detection of Left-to-Right Shunts

E. Braunwald, A. Goldblatt, R. T. L. Long, and A. G. Morrow. *British Heart Journal [Brit. Heart J.]* 24, 47–54, Jan., 1962. 5 figs., 10 refs.

The radioactive krypton (85Kr) inhalation test was used at the National Heart Institute, Bethesda, Maryland, during right heart catheterization in 161 patients with

proven left-to-right cardiac shunt and in 162 patients. without such shunt, most of the latter having rheumatic valvular heart disease, while a few had isolated pulmonary stenosis and others had no cardiac abnormality. The tank containing 85Kr (0.4 µc. per litre of air) was connected through a demand valve to a mouthpiece from which the mixture was inhaled for 30 seconds. Simultaneous sampling of blood from the cardiac catheter and from a systemic artery was carried out between the 10th and 13th seconds of inhalation and the radioactivity in these samples immediately determined in a continuousflow Geiger-Müller tube attached to a decade scaler; after subtraction of the activity in previously obtained blood samples for background activity the ratio of radioactivity in blood from the right heart to that in blood from the systemic artery was expressed as a percentage. In many patients sampling was performed at various sites in the right heart in successive tests.

In the patients with a left-to-right shunt this ratio varied from 13 to 113%, whereas in the patients without cardiac shunt it varied from 0 to 12% (average 3.6%). Incompetence of the pulmonary or tricuspid valve could lead to error in locating a left-to-right shunt and the test was also found to be of less value in defining the distal shunt when multiple left-to-right shunts were present.

K. G. Lowe

1389. The Normal Resting Cardiac Output: Serial Determinations by a Dye Dilution Method

T. A. BRUCE and J. P. SHILLINGFORD. British Heart Journal [Brit. Heart J.] 24, 69-75, Jan., 1962. 4 figs., 24 refs.

The introduction of "Coomassie" blue dye and the development of a photoelectric earpiece giving a linear response to concentration of the dye have now made it possible to make reliable serial determinations of cardiac output without cardiac catheterization and arterial puncture. At the Postgraduate Medical School of London 3 to 8 serial dye-dilution curves were obtained at 5-minute intervals after injection of 25 mg. of 1% Coomassie blue dye from 11 physicians and 12 ambulatory hospital patients with normal cardiovascular systems, the results being recorded on a Mark II Cambridge dye recorder with a high-resistance input circuit. Since the cardiac output is inversely proportional to the area under the recorded curve it is possible to estimate changes in cardiac output from the changes in the curve areas.

Only 6 subjects maintained a relatively stable output throughout the period of study. The average value for the group of physicians showed no significant change between the first and second series of determinations, whereas in the group of patients there was an average fall of 7% in the second series, suggesting that in these subjects the initially high cardiac output had been due to apprehension, though considerable trouble had been taken to explain the procedure and reassure the patients beforehand. The average standard error of the mean in all subjects was $\pm 6\%$ for all determinations and $\pm 3\%$ for the last four determinations for each individual. The average change in cardiac output for the whole group over the total series of determinations did not exceed 7%.

1390. The Spatial Vectorcardiogram in Proven Atrial Septal Defect

H. ABRAMSON and C. R. BURTON. British Heart Journal [Brit. Heart J.] 24, 103-109, Jan., 1962. 3 figs., 10 refs.

The differentiation of an ostium secundum from an ostium primum defect of the atrial septum is now of clinical importance, since surgical closure of the former is considerably less complicated. Working at the General Hospital, Toronto, the authors, using two channels of a multi-channel photographic recorder and the 7-lead system described by Frank (Circulation, 1956, 13, 737) have recorded the vectorcardiogram in 30 patients with atrial septal defect, confirmed in 29 cases by open heart surgery and in one by post-mortem examination. There were 23 cases of ostium secundum defect with a well defined inferior rim above the atrio-ventricular valves, associated in 7 cases with anomalous pulmonary venous drainage, in 2 with mitral stenosis, and in 3 with mitral incompetence. Two patients had complete A-V communis defect and 5 had the incomplete form of ostium primum defect.

Two distinctive vectorcardiographic patterns were observed in the frontal plane. In the cases of ostium secundum defect there was clockwise rotation of the QRS Es loop, with most of the loop inscribed below the iso-electric point. In the cases of ostium primum defect and complete A-V communis defect there was counterclockwise inscription of the loop, most of which was above the iso-electric point. This difference in pattern could not be explained by the presence or absence of mitral incompetence and the authors agree with the view that the pattern of the loop in ostium primum defect is due to an associated abnormality of the conducting system of the ventricles. Distinctive patterns for the two types of atrial septal defect were not found in the horizontal plane projection. K. G. Lowe

CONGENITAL HEART DISEASE

1391. Twins and Congenital Heart Disease. [In English]

M. CAMPBELL. Acta geneticae medicae et gemellologiae [Acta Genet. med. (Roma)] 10, 443-455, Oct., 1961 [received Jan., 1962]. 28 refs.

The author has studied the families of 942 propositi suffering from ventricular septal defect, atrial septal defect, simple pulmonary stenosis, patent ductus arteriosus, or coarctation of the aorta, most of whom were seen as Guy's Hospital, London. Among the 2,801 children of these families there were 38 multiple births, 37 pairs of twins and one set of triplets. In 16 pairs of twins one member was affected with a congenital cardiac defect, but in no case were both members affected. In 5 other pairs one infant was affected but the condition of the twin was not known, while in a further 2 pairs the condition of neither member was known because of early death. Both members of the remaining 15 pairs were normal.

The sex distribution in the affected pairs was unusual in that both members were of the same sex in 14 cases and of different sex in only 2. The zygosity of these twins was not known, but it is suggested that such preponderance of like sex suggests that there was an increased proportion-of monozygous twins among pairs of which one member had a congenital cardiac defect. The authorquotes Lamy et al. (Amer. J. hum. Genet., 1957, 9, 17) and Uchida and Rowe (ibid., 1957, 9, 133) to the same effect. He concludes that both a genetic factor and an environmental factor may be necessary before a congenital defect of the heart becomes manifest in one twin. If it is shown to be true that such twins are usually monozygous the environmental factor may be related to the common placental circulation, the affected member receiving either less or more blood than the unaffected H. G. Farauhar one.

1392. Aortic-valve Atresia: Report of 43 Cases D. G. Watson and R. D. Rowe. Journal of the American Medical Association [J. Amer. med. Ass.] 179, 14-18, Jan. 6, 1962. 2 figs., 9 refs.

The authors describe 43 cases of atresia of the aortic valve seen in the 7-year period 1952-8 at the Hospital for Sick Children, Toronto, in 24 male and 19 female infants whose average age at death was 4½ days. This condition contributed 23% of all deaths at the hospital from congenital heart disease in the newborn period. The chief features were dyspnoea, cyanosis, and cardiac failure, cyanosis appearing at an average age of 2 days. In 23 out of 39 cases there was a soft pulmonary systolic murmur with an accentuated single second sound, and in 3 recent cases an ejection click was heard. The blood pressure was uniformly low, averaging 65/45 mm. Hg; it was unrecordable in 6 cases and femoral pulsation was impalpable in one-third of the cases. In a similar proportion gallop rhythm, usually apical, was heard.

Radiographs showed the heart to be enlarged; in onethird it was globular in shape and in one-half suggestive of a truncus arteriosus. Though pulmonary plethora was not marked, pulmonary oedema could be detected in most of the cases. In two cases retrograde aortograms demonstrated the diminutive ascending aorta, the coronary arteries, a patent ductus arteriosus, and the pulmonary arteries. Electrocardiography showed peaked P waves, a normal or right QRS axis, evidence of right ventricular hypertrophy (in a few cases combined with left ventricular hypertrophy), and often Q waves in right precordial leads. At necropsy the right atrium was found always to be large and the left atrium small. These chambers were usually connected by a patent foramen ovale or other septal defect, but in 3 cases there was no channel of communication between the pulmonary veins and the right side of the heart. The mitral valve was small in all cases and atretic in 9. The left ventricle was a small cleft in the upper left ventricular mass and in 17 cases showed evidence of endocardial fibroelastosis which affected the left atrium in 4. Development of the aortic valve varied from complete absence to a dome-like imperforate diaphragm. The coronary arteries arose normally; the ascending aorta in all cases was hypoplastic with an average circumference of 5 mm. and at the arch of 9 mm. The pulmonary artery was always large, arose

from a dilated rather than hypertrophied right ventricle, and ran smoothly into a large ductus arteriosus supplying a normally sized descending aorta. In 11 cases extracardiac abnormalities, mainly minor urogenital defects, were also found.

In the immediate neonatal period the condition was confused with the pulmonary distress syndrome and with birth injury. Preductile coarctation of the aorta, a large patent ductus arteriosus, and a truncus arteriosus may all present with cardiac failure at the same age, but in these conditions the cyanosis is less. Transposition of the great vessels may also cause confusion, but here the "egg-shaped radiograph" and venous angiography help to differentiate this anomaly. A single ventricle and mitral atresia can similarly be distinguished. Those rare cases with evidence of left ventricular-hypertrophy in the electrocardiogram may be confused with tricuspid valvular atresia and pulmonary atresia, but the former can be detected by venous angiography and the latter recognized by the oligaemic lung fields. However, aortic atresia cannot be distinguished on clinical grounds from severe aortic stenosis. The authors emphasize the following points in diagnosis: (1) early cardiac failure with cyanosis; (2) an accentuated single second pulmonary sound; (3) a pulmonary flow murmur with an ejection click; and (4) weak peripheral pulses and a low blood pressure. The prognosis is hopeless, but correct diagnosis is important in order to detect those other conditions with which aortic valve atresia may be confused, and which are amenable to surgery.

H. G. Farquhar

1393. Left Superior Vena Cava: a Review of Associated Congenital Heart Lesions, Catheterization Data and Roentgenologic Findings

R. S. Fraser, J. Dvorkin, R. E. Rossall, and R. Eidem. American Journal of Medicine [Amer. J. Med.] 31, 711-716, Nov., 1961. 3 figs., 10 refs.

Persistence of the embryological left anterior cardinal vein and left duct of Cuvier results in a left-sided superior vena cava, usually entering the coronary sinus, blood being discharged into the right atrium. It may also receive a left-sided accessory hemiazygos vein, thus draining the left side of the chest as well as the left side of the head and the left arm. A right-sided superior vena cava may coexist, with a varying degree of intercommunication between the two vessels.

The authors of this paper from the University of Alberta and University Hospitals, Edmonton, Canada, have encountered 30 cases, mainly on cardiac catheterization, among some 700 cases of congenital heart disease (4.3%). In 5 cases the left superior vena cava discharged into the left atrium, causing cyanosis. Various other congenital anomalies were associated, the commonest being atrial septal defect and the tetralogy of Fallot. In 15 cases the abnormal vessel could be identified on a plain radiograph as a crescentic shadow at the extreme apex of the left lung, running down towards the upper left hilum.

It is pointed out that a left superior vena cava complicates cardiac catheterization, making entry into the pulmonary artery virtually impossible, and that the incidence of arrhythmia following catheterization is higher than in other cases. Supraventricular tachycardia occurred in 38% of the present series, compared with a usual incidence after catheterization of 8%. A left superior vena cava also complicates surgery; it may be ligated if there is adequate cross-connexion with a right superior vena cava, or it may be transplanted into the right atrium if its entry into the left atrium is causing cyanosis.

J. A. Cash

1394. Cardiac Malformation in Mongolism: a Prospective Study of 184 Mongoloid Children

R. D. Rowe and I. A. Uchida. American Journal of Medicine [Amer. J. Med.] 31, 726-735, Nov., 1961. 3 figs., 17 refs.

The incidence of cardiac malformation in mongolism was studied in 184 mongol children referred to the Hospital for Sick Children, Toronto, between July, 1955, and June, 1957. This series was considered truly representative of local mongol births and included 124 children aged under one year. A family history was obtained in 142 cases and revealed that in 10 families there was a second mongol and that in 4 of these there were mongol siblings. The maternal age in these 4 families was below the over-all average of 33.5 years.

The cardiac state was assessed at catheterization where permitted (55 cases), at repeated clinical examination, or at necropsy. Excluding 10 children whose cardiac state was uncertain, 70 (40%) had cardiac defects which, in order of frequency, included: atrioventricular canal defects, 25 patients (22 with atrioventricularis communis and 3 with ostium primum defect); ventricular septal defect, 23; patent ductus, 7; atrial septal defect (secundum type), 6; isolated aberrant right brachial artery, 5; other defects, 4. It is pointed out that the figure of 40% with cardiac abnormalities is lower than that reported in the literature, possibly because the present series was more truly representative than others and included many milder cases.

The follow-up study continued for a further 2 years, by which time 53 children had died, most of them from infections. Of these 53 patients, nearly all 6f whom were under 2 years of age, 32 had cardiac abnormalities, indicating the poor prognosis where mongolism and cardiac defects coexist.

J. A. Cosh

1395. Isolated Right Ventricular Hypoplasia with Atrial Septal Defect or Patent Foramen Ovale

M. A. SACKNER, M. J. ROBINSON, W. L. JAMISON, and D. H. LEWIS. *Circulation [Circulation]* 24, 1388–1402, Dec., 1961. 11 figs., 16 refs.

It was formerly stated that right ventricular hypoplasia is always associated with underdevelopment or malformation of the tricuspid or pulmonary valves, but 4 cases of hypoplastic right ventricle unassociated with valvular defects but with an accompanying patent foramen ovale or atrial septal defect have been reported in recent years. All these were in cyanotic infants or young children. The anomaly has also been recorded in certain cases of transposition of the great vessels. The authors here report 3 adult cases of hypoplastic right ventricle and

also a case in a child of 2 months in which an isolated right ventricular hypoplasia was found at necropsy. The 3 adults were members of one negro family, and in them the lesion was associated with an atrial septal defect and its distinctive clinical and haemodynamic features.

R. Wyburn-Mason

VALVULAR DISEASE

1396. The Results of Operation in Combined Mitral and Aortic Stenosis

M. HONEY. Guy's Hospital Reports [Guy's Hosp. Rep.] 110, 287-298, 1961. 1 fig., 16 refs.

Thirty-two patients operated on for combined mitral and aortic stenosis without significant incompetence of either valve pre-operatively have been followed up for between 2 and 9 years. There were 3 operative deaths, 2 further patients died in the first year and 6 more died later. Seventeen patients obtained a good early result, but only 10 patients (less than one-third) still had a good result at the end of the period of observation. The results were not appreciably better in the group in whom mitral and aortic valvotomy (21 patients) were undertaken than in the smaller group (11 patients) who had mitral valvotomy alone. It is clear that in a relatively small proportion of patients with combined mitral and aortic stenosis, satisfactory relief of both stenoses can be achieved, with ensuing good symptomatic result. However, the overall results in this series have been conspicuously less good than in lone mitral stenosis and less good even than in severe lone aortic stenosis. This can be attributed to the following observations: these patients have relatively advanced multivalvular rheumatic heart disease; in the presence of aortic valve disease, the production of mitral incompetence at operation is of. especially serious significance; relief of aortic stenosis when the valve is uncalcified, as is usually the case in these patients, is particularly likely to be followed by aortic incompetence. Future improvement in the treatment of these patients should occur with the development of satisfactory and reliable techniques of valve repair or replacement under direct vision, using extracorporeal circulation.—[Author's summary.]

1397. The Effect of Exercise upon the Mean Systolic Left Ventricular-Brachial Artery Gradient in Aortic Stenosia

P. SAMET, W. H. BERNSTEIN, and R. S. LITWAK. Diseases of the Chest [Dis. Chest] 40, 665-671, Dec., 1961. 7 figs., 2 refs.

The effect upon the aortic pressure gradient of varying cardiac output by exercise was studied at Mount Sinai Hospital, Miami Beach, Florida, in 4 patients with aortic stenosis. It was considered that the findings might help in the evaluation of the mechanism of dyspnoea of effort, angina, and syncope in aortic stenosis. Right heart catheterization, brachial artery canulation, and posterior percutaneous left atrial puncture were carried out in each patient and cardiac output was determined by the Fick principle. The left ventricular-brachial artery gradient was calculated by planimetric integration of the

systolic pressure difference between the left ventricular and brachial artery pressure curves.

In 3 of the patients there were significant flow increases during exercise but in all 4 there were only small rises in the aortic systolic gradient.

D. Goldman

1398. The Significance of Gas Metabolism Tests after Exertion in the Differential Diagnosis of Mitral Stenosis and Incompetence. (Значение изучения газообмена при физической нагрузке в дифференциальной диагностике митрального стеноза и митральной недостаточности)

. А. М. Damir and I. F. Martynov. Терапевтический Архив [Ter. Arh.] 33, 17-23, Dec., 1961. 1 fig., 4 refs.

The authors have measured the pulmonary ventilation and oxygen consumption in 23 patients with pure mitral stenosis, 20 with pure mitral incompetence, and 17 healthy control subjects before, immediately after, and again 10 minutes after a fixed exercise consisting of 20 ascents and 20 descents of an 18-cm, step per minute for 2 minutes. In the cardiac patients the diagnosis was made in some cases clinically with the aid of modern techniques, but in others only at operation.

In the controls the oxygen consumption rose by an average of 48% and the pulmonary ventilation by 70%, returning to normal in 10 minutes. In the patients with mitral stenosis pulmonary ventilation rose to 265% of the resting rate during exercise, but the oxygen consumption fell by 20%. In those with pure mitral incompetence the pulmonary ventilation rose to 182% of the volume at rest, while the oxygen consumption rose by 34%. Furthermore, all the patients with mitral incompetence showed normal oxygen consumption and all but 4 had a normal minute volume at the end of 10 minutes' rest, whereas in none of those with mitral stenosis did these values return to normal within that period. The authors consider that these tests are of considerable value in assessing the degree of stenosis and of the relative importance of stenosis and incompetence in mixed cases. particularly when weighing the indications for and against mitral commissurotomy. L. Firman-Edwards

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1399. Clinical Evaluation of Propatylnitrate in Angina Pectoris

G. SANDLER. British Medical Journal [Brit. med. J.] 2, 1741-1744; Dec. 30, 1961. 8 refs.

This paper from the City General Hospital, Sheffield, reports a trial of propatylnitrate ("gina") in 13 patients with angina pectoris. A double-blind technique was used, and both the immediate and prolonged action of the drug were studied, its effects being compared with those of placebo tablets as well as pentaerythritol tetranitrate ("mycardol") and glyceryl trinitrate. Propatylnitrate was found to bring rapid relief in acute attacks of angina. There was no evidence to show that it had a prophylactic prolonged action as a coronary vasodilator. It is concluded that the drug could be useful in treating

patients who experience unpleasant side-effects with trinitrin or who have become resistant to that drug.

A. I. Suchett-Kaye

1400. Coronary Disease among Professional People. (Коронарная недостаточность у пиц умственного труда)

É. É. Krister, O. N. Beliaeva, V. V. Goldina, T. K. Gurskala, and A. I. Leščenko. Клиническая Медицина [Klin. Med. (Mosk.)] 39, 3-6, Dec., 1961.

The authors present the results of a comparative study of the incidence of coronary arterial disease among members of two scientific institutions, namely, the Institute of the Food Industries (I.F.I.) and the Institute of Geology (I.G.). There is a marked difference in the activities and habits of the members of these two institutions. Thus the members of the I.F.I. are, apart from research work, also engaged in teaching, their working hours are longer (up to 12 hours a day), 27.8% of them have not enough sleep (as against 12.8% among members of the I.G.), they walk less, they rest less during their vacations, pay less attention to their diet (48.4% as compared with 15.8% among I.G. members), and lastly a larger proportion of them smoke (39.1% as against 24.7% among members of the I.G.).

Of the 102 employees of I.F.I. under the age of 60 years, 33.7% suffered from coronary arterial disease, whereas of the 147 members of the I.G. of similar age, only 16.8% suffered from this disorder. In both institutions the proportion of laboratory assistants and technicians with coronary disease was only about 4%. The study also showed incidentally that the incidence of coronary disease was much higher among smokers than among non-smokers.

A. Orley

1401. Serum Lactescence in Normal Subjects and in Patients with Coronary Artery Disease before and after the Administration of Sublingual Heparin

M. A. PEYMAN. American Heart Journal [Amer. Heart J.] 62, 676-679, Nov., 1961. 16 refs.

The claim that heparin administered sublingually is effective in clearing the turbidity of hyperlipaemic serum without interfering with the blood clotting mechanism was investigated at Charing Cross Hospital, London, in 40 healthy subjects (32 men and 8 women) and in 25 patients (21 men and 4 women) with myocardial infarction which had occurred within the previous 6 weeks. Samples of blood for determination of serum lactescence were taken from each individual after fasting for at least 9 hours and also at 2, 3, 4, 5, and 6 hours after a standard meal of fat, which in 25 cases consisted of 3 oz. (85 ml.) of a lipid emulsion and in 40, including all the patients with myocardial infarction, of a mixture of 4 oz. (114 ml.) of milk and 4 oz. of "double" cream, equal to 60 g. of fat. The optical densities of the centrifuged citrated serum were measured by means of a Spekker spectrophotometer (using a red filter at a wave-length of 740 m μ). The whole procedure was then repeated within a period of one week, but on this occasion each subject received one tablet of heparin (1,500 units) by sublingual administration immediately after the meal, another tablet one

half-hour after the meal, and a third one hour after the meal, a total of 4,500 units of heparin.

In both healthy subjects and in the patients the mean values for serum turbidity were unaltered by the sublingual administration of heparin. Furthermore, in 10 of the healthy subjects the clotting time of the blood (by the method of Lee and White) in the fasting state and at 3 and 5 hours after the fatty meal was unchanged, suggesting that heparin is not substantially absorbed by this route.

This study also confirmed that, compared with the findings in normal subjects, in patients with myocardial infarction a more pronounced lipaemia follows the ingestion of fat.

Eirian Williams

1402. Epigastric Distress in Patients with Earlier Myocardial Infarction. [In English]

T. VARTIO. Annales medicinae internae Fenniae [Ann. Med. intern. Fenn.] 50, 239-245, 1961. 24 refs.

Of 397 patients who had had myocardial infarction and were readmitted to the Provincial Hospital, Oulu, Finland, 8.5% had epigastric discomfort as the main symptom when re-examined. Investigation showed that gall-bladder disease accounted for 5% and hiatus hernia for 1.2% of these cases. Of another group of 42 with coronary disease, who were later admitted to hospital with severe epigastric discomfort, gall-bladder disease was found in 8 (19%), peptic ulcer in 9 (21.4%), and hiatus hernia in 2 (4.7%). In 6 of the patients with peptic ulcer this condition was present before the myocardial infarction.

The study confirms the well-recognized association between coronary and gall-bladder disease and suggests a stress link between coronary disease and peptic ulceration.

T. Semple

1403. Clinical Observations on the Cause of Death from Myocardial Infarction with Reference to 100 Cases of Coronary Thrombosis. (Remarques cliniques sur les circonstances de la mort au cours de l'infarctus du myocarde d'après 100 observations de thrombose coronarienne)

M. DEPARIS, G. MANIGAND, and P. BRUNET. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 38, 107-115, Jan. 8, 1962. 5 figs.

Of 100 patients admitted to the Höpital de Bicêtre, Paris, with coronary thrombosis, 32 died within 2 months. In this series of patients 77 were men, 23 women, and 85% were over 50 years of age. The 100 patients had a total of 116 incidents of myocardial infarction and their clinical presentation was as follows: typical, with prolonged pain 73 cases (62-9%); anginal pain only 16 (13-9%); atypical, without pain 10 (8-6%); and latent 17 (14-6%).

Of the 10 patients with painless infarction; 5 presented with heart failure, 2 with haemoptysis, and 3 with cerebral embolism. Of the 32 patients who died, 14 had heart failure and 9 cardiovascular collapse. In 15 of these death occurred suddenly; rupture of the heart, irregularities of rhythm, recurring infarction, and pulmonary embolism were found in 7 patients, but in

the other 8 the cause of sudden death remained unexplained. One of the characteristic features of myocardial infarct is the uncertainty of the prognosis: thus of 16 patients with a so-called benign presentation, 4 died. Among unfavourable prognostic factors noted were advanced age, previous heart failure, and intensity or long duration of the pain. Of 16 patients who had a history of previous myocardial infarction, 10 died.

A. J. Karlish

1404. Variations in the Serum Iron Level in Patients with Acute Myocardial Infarction. (Колебания, сывороточного желева у больным острым инфарктом миокарда)

M. I. ZOLOTOVA-KOSTOMAROVA and L. R. NOZDRJUHNA. Tepaneemuveckuŭ Apxue [Ter. Arh.] 33, 42-51, Dec., 1961. 17 refs.

The role of iron in the biological processes of the body is not confined to blood formation, but iron also plays a part in the synthesis of enzymes such as catalase, peroxidase, and cytochrome. The serum iron level varies considerably in intoxications, infections, and inflammatory processes generally, as well as in hypoxia, and the values in these conditions reported by various authors are quoted.

In the present investigations 71 cases of myocardial infarction (29 of coronary thrombosis and 43 of atherosclerotic occlusion) were studied, but this paper deals only with the former group. The cases were divided as follows: (1) 16 with a favourable outcome; (2) 6 severe cases with repeated attacks of pain, subfebrile temperature, and blood changes; (3) 3 with a background of chronic coronary insufficiency; and (4) 4 cases which ran a very severe and prolonged course, with cardiac aneurysm and acute attacks of cardiovascular distress, but with periodical remissions.

In Group 1 hyperferraemia occurred from the onset, the serum iron level reaching 224 to 308 μ g. per 100 ml. and falling to normal after 7 to 9 weeks. In Group 2 the serum iron level was normal at first, but then gradually rose to reach a high level (336 μ g. per 100 ml.) in cónvalescence, thereafter slowly falling to normal levels. In Group 3 the level fell sharply to a very low value (28 μ g. per 100 ml.) on the 4th day after onset and remained low for several months. In Group 4, the iron level was consistently low (28 μ g. per 100 ml.) except during remissions. It is considered that these changes suggest that the mobilization of iron is related to the state of the circulation in general and particularly to the blood supply to the lungs. liver, and gastro-intestinal tract. Mobilization of ironoccurs as a positive reaction to sudden onset of hypoxia. while replenishment depends upon adequate circulation to the alimentary tract. L. Firman-Edwards

1405. Cardiac Infarction and the Glucose-tolerance Test E. Sowron. *British Medical Journal [Brit., med. J.]* 1, 84-86, Jan. 13, 1962. 1 fig., 5 refs.

In 30 patients (22 male and 8 female) admitted to King's College Hospital, London, with a recent myocardial infarction oral glucose tolerance tests were carried out in the acute phase of the illness, usually on the day

following admission. Known diabetics and obese patients were excluded. In 15 of the patients the glucose tolerance curve was diabetic, in 8 it was normal, and in 7 it was intermediate and classified as "abnormal". After 6 months the curve was diabetic in only 3, "abnormal" in 10, and normal in 17. In 19 the curve had improved and in 7 it had deteriorated. The pattern of the curves did not correlate with the serum cholesterol level nor with any alteration in body weight. Of 20 "control" patients from the same wards, matched for age and sex, the curve was normal in 17, only 3 showing an "abnormal" pattern.

A group of 13 patients with myocardial infarction

A group of 13 patients with myocardial infarction were followed up for 3 to 5 years. In the acute phase 4 had diabetic and 4 had "abnormal" curves. At the time of follow-up clinical diabetes had developed in 2, only one of whom previously had an "abnormal" curve, and 2 had "abnormal" curves (one previously diabetic and one normal).

The author discusses the causes of this impaired glucose tolerance which is seen immediately after myocardial infarction and often persists for some time. The hypotheses which he tends to discard include increased adrenocortical steroid production, circulatory disturbances in the hypothalamus or liver, adrenaline-induced glycogenolysis, and low carbohydrate intake He favours the view that the cardiac infarction precipitates latent diabetes.

T. B. Begg

1406. Factors in Myocardial Rupture: an Analysis of Two Hundred and Four Cases at Los Angeles County Hospital between 1924 and 1959

G. C. GRIFFITH, B. HEDGE, and R. W. OBLATH. American Journal of Cardiology [Amer. J. Cardiol.] 8, 792-798, Dec., 1961. 1 fig., 22 refs.

Between 1924 and 1959 some 57,000 routine necropsies were performed at Los Angeles County Hospital, California, and of these, 3,103 (5.5%) revealed hearts with one or more unhealed infarcts. In 215 instances infarction had been followed by rupture and the 204 cases here discussed represent those for which adequate detailed information was available. All but 2 of the patients were over 50 years of age. Contrary to expectation the incidence of rupture in women (110 cases) slightly exceeded that in men (94), but the difference was not significant. As to racial differences, although about one-third of the patients admitted to this hospital are negroes, the 129 cases in which race was recorded included only 3 negro patients (2.3%).

The infarcts occurred most commonly in the anterior descending branch of the left coronary artery and the great majority of the ruptures took place in the left ventricle, usually on the anterior surface, the most common site being the junction of the anterior wall with the septum; in all cases the rupture was at or immediately adjacent to the site of necrosis. No atrial or interatrial ruptures were found in this series. Ante-mortem electrocardiograms taken during the acute episode of infarction were available in 35 of the cases. One tracing appeared to show no abnormalities, but in most of the others the indications were in keeping with the post-mortem find-

ings. The survival period and survival rate were inversely related to the number of hours elapsing between the clinical onset of infarction and admission to hospital. Although in cases of ventricular rupture death was usually immediate, rupture of the septum was much less catastrophic. In the pathogenesis of rupture the most important factors—apart from the degree of damage done by the infarct—appeared to be stress and hypertension. The hazard was considerably greater in small hearts.

During the 35 years covered by the survey the incidence of unhealed infarction disclosed at necropsy rose from 2.1 to 7.6% and throughout most of the period the incidence of rupture followed a parallel course. During the last 8 years, however, the latter has shown a sharp decrease, presumed by the authors to be due to the better management of the acute phase of the illness and particularly to the use of vasopressor and anticoagulant drugs. They found from the clinical histories that cardiac tamponade (pulsating neck veins with increasing cardiac dullness) is a relatively frequent accompaniment of rupture in patients receiving anticoagulants, and recommend special alertness for this feature in view of the improved chances that this may now be dealt with. surgically. Details of a number of illustrative cases are included:-

[An unusual paper, which is well written and in which the conclusions are both logical and enlightening.]

Rex Matthews

1407. Acute Myocardial Infarction in a City Hospital. V. Follow-up Study of One Hundred Thirty-one Survivors B. A. Rosenberg and M. Malach. American Journal of Cardiology [Amer. J. Cardiol.] 8, 799-806, Dec., 1961. 26 refs.

A 5-year follow-up study of 131 survivors of acute myocardial infarction in a city hospital during a 1-year period is presented. The mortality rate was 28% at 1 year and 49% at 5 years. Seventy per cent of the deaths occurred in the hospital. Eighty-eight per cent of deaths were due to recurrent myocardial infarction and/or congestive heart failure. Pre-existing hypertension, angina pectoris, or congestive heart failure, location of the acute infarction or cardiomegaly during hospitalization, did not significantly affect the long range outcome. Previous myocardial infarctions adversely affected the 5-year survival rate of the acute infarction.

Pre-existing angina pectoris was absent in one-fourth of cases 3 and 5 years after discharge, while pre-existing hypertension disappeared in one-half at 3 years and one-fourth at 5 years. Angina pectoris appeared for the first time in over half of the patients by 3 and 5 years after discharge. Hypertension was first noted in 25% of patients at 3 years and 50% at 5 years. Congestive heart failure was demonstrated objectively in 68% of the cases at 3 years and 33% at 5 years. Cardiomegaly was noted roentgenographically in 46% at 3 years and 77% at 5 years and was apparently associated with coronary artery disease alone in 8% and 28% respectively. The electrocardiogram revealed no evidence of infarction in 13% at 3 years and 20% at 5 years.—[Authors' summary.]

BLOOD VESSELS

1408. Platelet Adhesiveness in Normal Persons and Subjects with Atherosclerosis. Effect of High Fat Meals and Anticoaculants on the Adhesive Index

L. HORLICK. American Journal of Cardiology [Amer. J. Cardiol.] 8, 459-470, Oct., 1961. 6 figs., 36 refs.

In this study reported from the University of Saskatchewan, Canada, platelet adhesiveness (platelet stickiness) was measured in 53 healthy subjects (49 male and 4 female, average age 42.4 years) and in 52 patients (49 male and 3 female, average age 57.7 years) with coronary arteriosclerosis. The method of Moolten and Vroman was employed, in which venous blood is drawn into citrated siliconized syringes, erythrocyte and platelet counts are made, and the ratio of erythrocytes to platelets is determined. An aliquot of blood is then passed through a specially prepared "fiberglas" filter and washed through with saline. Counts are made on the filtrate and the "adhesive index" is obtained by dividing the ratio of erythrocytes to platelets after filtration by the ratio obtained before filtration. The mean adhesive index in the normal subjects was 1.06, and it appeared to be uninfluenced by age, the value for those over the age of 40 years being the same as that for those under 40; in 3 of the healthy subjects aged 28, 29, and 53 years respectively the adhesive index was 1.19 or greater. In the patients with coronary arteriosclerosis the mean adhesive index was 1.11, and in 16 a value of 1.19 or greater was obtained. The results of multiple determinations showed that there was less day to day variation in the normal subjects than in patients with coronary arteriosclerosis.

The findings in the patients were therefore analysed further. In 25 cases studied within 12 months of an attack of myocardial infarction the mean adhesive index was 1.11, in 15 studied within 4 weeks of infarction the index was also 1.11, in 14 patients suffering from angina pectoris it was 1.16, and in 13 in whom an interval of freedom of more than a year had followed an attack ofmyocardial infarction the mean adhesive index was 1.05, closely similar to that in normal subjects. In 39 patients studied within 12 months of myocardial infarction who complained also of angina the mean adhesive index was 1.14, the difference from the normal value being highly significant. This finding suggested that the "adhesive tendency" may be a temporary phenomenon occurring during an active stage and not seen in the stabilized patient with arteriosclerotic heart disease.

In a further test the adhesive index in 25 normal subjects and 25 patients with coronary arteriosclerosis was measured in the fasting state and at 2, 4, and 6 hours after a breakfast containing 75 g. of animal fat. The fasting index values were higher in the patients with coronary arteriosclerosis; and while in all normal subjects the initial values remained unchanged, in 11 of the patients with coronary arterial disease the fatty meal induced a further increase in the adhesive index. The effect of the anticoagulants "sintrom" (nicoumalone) and "danilone" (phenindione) on the adhesive index was then studied in 24 patients with coronary arteriosclerosis. In

13 of them the index increased significantly, generally during the first 72 hours of anticoagulant treatment. Dicoumarol in small doses (100 mg. daily) was given to 9 patients and a rise in the adhesive index was noted in 5, suggesting that the effect of anticoagulant drugs on the adhesive index is qualitative, since it caused a temporary hypercoagulable phase in over half the patients treated.

Eirian Williams

1409. Venous Tone

E. P. SHARPEY-SCHAFER. British Medical Journal [Brit. med. J.] 2, 1589–1595, Dec. 16, 1961. 13 figs., 17 refs.

After briefly referring to evidence suggesting that changes in peripheral venous tone occur in certain circumstances, the author of this paper from St. Thomas's Hospital Medical School, London, describes a method of measuring changes in tone in the forearm veins. Actually suitable segments of forearm veins occur in a few individuals only. The rate of rise in venous pressure and of increase in volume of a segment of forearm are recorded simultaneously when a proximal collectingcuff is inflated. [For experimental details and a discussion of the errors involved the original paper should be consulted.] Reflex constriction of the normal peripheral venous system occurs on tipping from the horizontal to the erect posture, with the Valsalva manœuvre, and following large venesections. Reflex venodilatation follows large cough transients and is abolished by interruption of reflex nervous pathways. Venodilatation also follows intravenous administration of ganglion blocking agents, indicating the presence of some resting tone in forearm veins. Adrenaline, noradrenaline, 5-hydroxytryptamine, and histamine are powerful venoconstrictors, while nitrites and isopropylnoradrenaline are venodilators. In heart failure, severe anaemia, and severe beri-beri venous tone increases.

R. Wyburn-Mason

SYSTEMIC CIRCULATORY DISORDERS

1410. Vasovagal Fainting: a Diphasic Response D. T. Graham, J. D. Kabler, and L. Lunsford Jr. *Psychosomatic Medicine [Psychosom. Med.*] 23, 493-507, Nov.-Dec., 1961. 8 figs., 22 refs.

An investigation of the mechanism of vasovagal fainting was carried out at the University of Wisconsin Medical School, Madison, particular emphasis being placed on the cardiovascular dynamics of the pre-fainting phase as well as of the fainting phase. Fainting was studied in (1) blood donors; (2) subjects who had a simple vene-puncture; and (3) patients undergoing air encephalography. In the first group (32 subjects) 10 faints occurred; in the second group (6 subjects) 7 faints; and in the third group (15 patients) 6 faints. Observations of cardiovascular variables were made before as well as during the faint. Systolic and diastolic blood pressure and pulse rate were recorded at intervals of 2½ to 3 minutes throughout the procedure; in addition, electrocardiographic recordings (Lead 2) were made.

The pre-fainting phase was characterized by a rapid or rising heart rate and increasing diastolic blood pressure, while the faint itself was accompanied by bradycardia and low blood pressure. Fainting can thus be regarded as a diphasic response in which the initial stage reflects anxiety and the later stage occurs as the result of sudden cessation of anxiety. It is pointed out that a physiological parallel exists between fainting and dying, some faints being marked by more or less prolonged asystole; furthermore, in 2 of the venepuncture-induced faints there was pronounced apnoea. It is suggested that other stress disorders, such as migraine and asthma, may be fruitfully regarded as diphasic responses.

A. Balfour Sclare

1411. Diagnosis and Treatment of Occlusive Renal Artery Disease and Hypertension

E. F. POUTASSE. Journal of the American Medical Association [J. Amer. med. Ass.] 178, 1078-1083, Dec. 16, 1961. 1 fig., 11 refs.

At the Cleveland Clinic, Ohio, during the 6 years 1955-60 inclusive, the author has employed abdominal aortography in the investigation of 617 patients with hypertension. Of these patients 167 were found to have occlusive disease of one or both renal arteries or their branches, and this paper describes the diagnosis and management of these patients together with a further 6 similar cases treated before 1955, making a total of 173 in all

No distinctive clinical pattern of hypertension was found in the patients with renal arterial occlusive disease. The sexes were equally represented, and the most frequent age range was 20 to 40 years. The only distinctive feature on physical examination was the presence of a systolic bruit, usually best heard over the upper abdomen. in about half the patients. Intravenous pyclography was found to be a valuable investigation for demonstrating the presence of renal arterial lesions, and 6 diagnostic signs are described which may be revealed by this method: (1) A non-functioning kidney which is morphologically normal on a retrograde pyelogram. (2) Delayed appearance of contrast medium on one side. (3) A difference in length of 1 cm. or more between the two kidneys. (4) Paradoxical hyperconcentration, that is, increased density of the dye shadow on the ischaemic side. (5) A smaller, more compact system of calyces on the affected side, reflecting the reduced urine flow., (6) Partial atrophy of one kidney due to occlusion of a branch of the renal artery. Differential studies of separate renal function, whether carried out by ureteric catheterization or by the use of radioactive isotopes, are not considered to be reliable as a screening test for the detection of renal arterial lesions, though they may provide valuable confirmatory evidence in selected cases.

The author describes his technique of renal angiography in detail. This is performed by the translumbar route, under local anaesthesia; the blood pressure is lowered to 100 mm. Hg systolic by hypotensive drugs; compression is applied to the lower abdomen; a small dose (10 ml.) of contrast medium is used, and a single, accurately timed, exposure is taken.

Of the 173 patients, 126 were treated surgically by a variety of procedures. Nephrectomy or segmental nephrectomy was at first the most common operation;

but with advances in technique and experience some form of arterial reconstruction with preservation of renal tissue is now more frequently used where this is technically feasible, provided that the kidney has not undergone advanced atrophy and the patient's condition is such as to withstand the more elaborate operation. Of the 126 patients treated surgically, 10 died postoperatively. In 44 out of 76 patients who were followed up for one year or more after operation, the blood pressure was normal. An additional 15 patients had some relief of their hypertension, though without return to normal blood pressure levels. In the remaining 17 patients there was no change in the blood pressure following surgery. In a few cases re-stenosis of the renal artery occurred months or years after resection, particularly in those patients with other than atherosclerotic lesions, that is, segmental mural M. Harington fibrosis or intimal sclerosis.

1412. Hypertension Secondary to Renal Artery Occlusive Disease

D. Perloff, M. Sokolow, B. J. Wylle, D. R. Smith, and A. J. Palubinskas. *Circulation [Circulation]* 24, 1286–1304, Dec., 1961. 6 figs., 39 refs.

The authors of this paper from the University of California School of Medicine, San Francisco, report their experience in the diagnosis and treatment of hypertension secondary to renal arterial stenosis. Over a recent 8-year period 110 hypertensive patients were subjected to renal arteriography, and half of these (54 patients) were found to have narrowing of one or both renal arteries severe enough to be considered as significant in relation to the hypertension.

The patients with renal arterial lesions did not differ "in their clinical appearance from the general population of hypertensive patients". In particular, the authors observations did not confirm the view that hypertension secondary to a renal arterial lesion was likely to be specially severe and difficult to control. In selecting patients for angiography the most useful indications were: recent onset or exacerbation of hypertension, a bruit audible over the renal arteries, disparity in the size of the two kidneys on pyelography, and clinical evidence of obliterative atherosclerosis. When a combination of these was present arteriography demonstrated a renal lesion in almost 100% of cases.

Operation was performed on 38 patients in an attempt to relieve the hypertension, either nephrectomy (8 patients) or an arterial reconstructive operation, most commonly endarterectomy. There were 7 deaths. Of the 31 survivors, 14 had normal blood pressure for follow-up periods of 2 months to 7 years (average 11 months). Some fall in blood pressure after operation, though not to normal, was observed in 11 other patients who on the average were slightly older and had a longer history of hypertension than those whose blood pressure fell to normal. In 6 patients there was no relief of hypertension after operation.

Pathological examination of the narrowed arteries of 24 patients who underwent operation and whose blood pressure fell revealed atherosclerotic plaques in 15. A separate group of 9 patients showed an arterial lesion of

fibromuscular hyperplasia, with intact intima; these patients were most commonly young women, usually with relatively benign hypertension. *M. Harington*

1413. The Role of the Kidney in Human Hypertension. I. Failure of Hypertension to Develop in the Renoprival Subject

J. P. MERRILL, C. GIORDANO, and D. R. HEETDERKS. American Journal of Medicine [Amer. J. Med.] 31, 931-940, Dec., 1961. 5 figs., 30 refs.

From the Peter Bent Brigham Hospital and Harvard Medical School, Boston, the authors describe their experience of the effect of total absence of renal tissue upon blood-pressure regulation in 4 human patients. Three of these were patients inadvertently deprived of a single kidney and the fourth underwent elective bilateral nephrectomy 10 days before renal transplantation from an identical twin.

The first patient had a blood pressure of 164/90 mm. Hg on admission and during the first week it ranged from this value up to 180/118 mm. Hg. The patient was judged on the basis of clinical findings and a serum sodium level of 129 mEq. per litre to be overloaded with fluid. Fluid restriction led to a fall in body weight and the blood pressure was below 145/80 mm. Hg for 45 days. The second patient was admitted with a blood pressure of 104/70 mm. Hg. A renal homograft was performed on the 23rd day, but the pressure remained below 120/80 mm. Hg until the 33rd day. It then rose to 160/100 mm. Hg and, during a convulsion, to 200/100 mm. Hg. Rigorous dehydration led to a fall in blood pressure to 120/90 mm. Hg until death on the 51st day. The third patient was admitted from Sweden after 31 days without renal tissue. The blood pressure was 112/58 mm. Hg and the highest value recorded in the next 10 days was 135/100 mm. Hg. During a grand mal seizure on the 19th day in Boston the pressure rose transiently to 140/110 mm. Hg. After dialysis and a 1.6 kg. weight loss the pressure fell to 134/74 mm. Hg and remained at or below that level until death. The fourth patient had acute glomerulonephritis and was admitted with a blood pressure of 130/90 mm. Hg. During a 10day period between bilateral nephrectomy and the successful transplantation of a kidney from an identical twin the blood pressure remained normal.

The authors conclude that renoprival hypertension does not occur in a man without kidneys if protein and salt are restricted and overhydration is avoided.

[These observations are of importance and strongly support the conclusions drawn from them. However, it is of interest, and still unexplained, why patients with bilateral nephrectomy respond with a rise in blood pressure to a moderate degree of overhydration.]

C. T. Dallery

1414. Hypertension—Sodium and Potassium Studies W. W. PRIDDLE. Canadian Medical Association Journal [Canad. med. Ass. J.] 86, 1-9, Jan. 6, 1962. 10 refs.

The effects of a low-sodium diet supplemented by potassium chloride (2 g. daily) and chlorothiazide (250 mg. daily, 5 days a week) were studied in 101 elderly

hypertensive patients (average age 58.4 years) seen at the Geriatric Study Centre, Toronto. Some of the patients were also receiving a low-animal-fat, low-cholesterol diet and some were receiving reserpine. Restriction of dietary sodium alone brought the urinary sodium: potassium ratio down from 1:2.46 (on unrestricted diet) to 1:2. With the full hypotensive regimen the ratio fell further to 1:0.79. The serum sodium level tended to be lowest on the full regimen, while the serum potassium level was lowest on sodium restriction plus chlorothiazide. The full regimen was associated with approximate mean falls of about 15 mm. Hg in systolic and about 12 mm. Hg in diastolic blood pressure. Patients generally felt improved in health on this regimen. Hypokalaemia presented no problem, but azotaemia occurred in the presence of renal damage and in some cases necessitated temporary omission of chlorothiazide. K. G. Lowe

1415. A New Antihypertensive Drug ("Mebutamate") in the Treatment of Refractory Hypertension in Geriatric Patients: Preliminary Report

C. H. LESLIE. Journal of the American Geriatrics Society [J. Amer. Geriat. Soc.] 10, 85-89, Jan., 1962, 3 refs.

A recently introduced hypotensive agent "mebutamate" (2-methyl-2 sec.-butyl-1:3-propanediol dicarbamate) was tried in the treatment of 17 "geriatric hypertensive patients" whose ages ranged from 41 to 92 (average 70·3 years). This compound has been reported as being effective in reducing blood pressure without producing untoward side-effects. Its action is said to be mediated through the central nervous system and not by direct action on the blood vessels or sympathetic ganglia. It is described as lowering blood pressure without decreasing cardiac output. From the figures given, mebutamate appears to be an effective hypotensive agent with very few side-effects and without any tendency to produce postural hypotension.

[This is a preliminary and not very useful report of a trial of a new substance which has been used on an extraordinarily heterogenous group of so-called elderly patients. It will need very much more careful appraisal before being accepted as enthusiastically as it is by the author.]

P. D. Bedford

1416. Clinical Trial of Methoserpidine in General Practice

D. L. B. H. Jones, A. M. MICHAEL, and J. P. OMMÉR. British Medical Journal [Brit. med. J.] 2, 1738–1741, Dec. 30, 1961. 12 refs.

A trial of methoserpidine ("decaserpyl") was carried out in general practice in Glasgow over one year on 48 patients suffering from hypertension and followed upfortnightly or monthly. Of 43 of the patients with essential hypertension the drug had a definite hypotensive effect in about two-thirds (29 cases). No side-effects were noted with the dosage used, that is, 10 to 60 mg. per day.

Methoserpidine appears to be a particularly safe hypotensive drug. It was found to be useful also in hypertension other than essential, especially in pre-eclamptic toxaemia.

A. I. Suchett-Kaye

Clinical Haematology

1417. Joint Symptoms in Myelomatosis and Similar Conditions

E. B. D. HAMILTON and E. G. L. BYWATERS. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 353-362, Dec., 1961. 7 figs., 9 refs.

Musculo-skeletal symptoms feature prominently in myelomatosis. The present authors show, in a detailed study of 46 cases of the disease, that bone pain was present in 42 and joint pain in 8 at some stage during the 10 years they were under the care of the Canadian Red Cross Memorial Hospital, Taplow, or the Hammersmith Hospital, London.

In all the cases the diagnosis was confirmed by sternal-marrow aspiration, tumour biopsy, or necropsy. Myoloma peaks were found on serum electrophoresis in 25 out of 34 patients, and Bence Jones protein was

present in 18 of 44 patients.

Bone pain was felt mostly in the lumbar or dorsal spine, and in the 8 cases in which joint pain was complained of this was in fact due to osteolytic lesions situated near the joints. Of those patients with joint disease, acute attacks of gout occurred in 2, degenerative joint disease was present in 3 (one also had gout), and one patient had para-amyloid infiltration of the carpal tunnel.

In addition to the 46 cases of proven myelomatosis, 6 cases in which serum protein abnormalities were present but myelomatosis was not confirmed are also described. Of 2 women whose blood was shown by electrophoresis to contain myeloma protein, one developed arthritis of the wrist-joints and hands and the other cervical arthritis. Macroglobulinaemia was excluded, and a synovial biopsy in the first patient revealed the presence of plasma cells typical of rheumatoid arthritis. Two further patients had macroglobulinaemia associated with polyarithritis; and in the remaining 2 patients a carpal tunnel syndrome and peripheral neuritis respectively were proved to be the initial manifestations of primary amyloidosis.

The authors mention in their discussion that amyloid deposition, which appears to be related in some undefined way with proliferation of plasma cells and increased or abnormal gamma globulin, may follow the protein abnormalities of rheumatoid arthritis and myelomatosis. In both conditions the plasma cells are increased in number, and macroglobulinaemia and myelomatosis may complicate rheumatoid arthritis. In 2 of the cases reported in the 2 of the cases reported in the patients' serum during the course of rheumatoid arthritis, though this might of course be coincidental. Another possibility is that the derangement of gamma globulin that occurs in myelomatosis may lead to a low level of normal globulin and an arthritis may develop similar to that seen in agammaglobulinaemia. The authors emphasize the importance of excluding myelomatosis

when amyloid is found to be present, and a case is cited which demonstrates the blurred frontier that may exist between the two conditions.

J. S. Malpas

1418. Clinical Patterns and Course of Anaemias in General Practice

J. FRY. British Medical Journal [Brit. med. J.] 2, 1732-1736, Dec. 30, 1961. 6 refs.

During the 5-year-period 1950-5 the author, in a practice of 5,000 patients with access to a hospital laboratory, recorded an annual incidence of anaemia of approximately 17.5 per 1,000 patients; during the same period 222 patients (44 male and 178 female) were seen in whom anaemia was the main clinical feature. The anaemia was hypochromic in 205 patients (92%) and "hyperchromic" in the remainder (pernicious anaemia 14, haemolytic anaemia 3). Of the patients with hypochromic anaemia, 82%, were females, and in 83% of these, most of whom were in the reproductive age, there was no obvious underlying cause, the anaemia being assumed, therefore, to be nutritional, perhaps with associated menorrhagia. No cause was apparent in 46% of the males with hypochromic anaemia, the anaemia in most of these cases occurring in infancy and early childhood. Alimentary haemorrhage was the most common cause in those cases in which an underlying disease was responsible. Most of the patients were managed at home; only 18 (8%) were referred to a consultant. Ferrous sulphate by mouth was the routine treatment in hypochromic anaemia, supplemented in severe cases by iron preparations intramuscularly; the intolerance rate was 20%.

Of 189 patients available for follow-up in 1959-60, 81% were still anaemic (Hb below 80%), and the majority of these were females between the ages of 30, and 60 in whom an underlying cause for the anaemia could not be found. Most of the relapses were attributed to failure to continue treatment, which, the author believes, should be maintained in such patients until well past the menopause. He emphasizes the need for hospital laboratory facilities to be available to general practitioners and the importance of long-term follow-up of these cases.

J. L. Markson

A. JA. JAROSEVSKII. Tepaneemuveckuu Apxus [Ter. Arh.] 33, 3-17, Dec., 1961. 3 figs., bibliography.

The amount of erythropoietins in the plasma and serum of 94 patients suffering from cardio-respiratory insufficiency (including 35 with bronchial asthma), 100 with various types of anaemia (including 29 with iron-deficiency anaemia), and 20 with renal disease was estimated by intravenous injection of their serum into

rats and rabbits and observing the resulting changes in the animals' blood and marrow. A group of 56 healthy controls were also investigated.

Patients with signs of oxygen lack due to respiratory and cardiac disease showed a significant increase in erythropoietins compared with normal controls, as shown by a rise in the reticulocyte and erythrocyte counts and increased activity of the bone marrow. The increase was not related directly to the degree of oxygen saturation of arterial blood and tended to be highest in cases of 2nd degree insufficiency. The rise in serum erythropoietin content in patients with vitamin-B₁₂ deficiency and in those with post-haemorrhagic anaemias was most noticeable at the height of the anaemia and fell during response to treatment; in the iron-deficient patients the rise reached its peak after 3 to 6 days' treatment and was much more marked if the serum was incubated with solutions of iron salts in a concentration of 100 μ g. per 100 ml. at 38° C, for one hour before testing. In the rats the marrow content of erythrocytes increased by 100% or more in some cases. In the patients with renal disease the results were inconclusive; owing to the numer: ous factors operating in these patients (for example, variations in the glomerular filtration rate or the presence of uraemia) further investigations are required in such cases. Some patients showed an increase and others a diminution in the serum erythropoietin content.

L. Firman-Edwards

1420. The Effect of "Minute" and "Titrated" Amounts of Folic Acid on the Megaloblastic Anemia of Tropical Sprue

T. W. SHEEHY, M. E. RUBINI, E. PEREZ-SANTIAGO, R. SANTINI JR., and J. HADDOCK. *Blood* [*Blood*] 18, 623-636, Dec., 1961, 5 figs., 36 refs.

The investigation reported in this paper from the University of Puerto Rico was designed to determine the minimum amount of folic acid necessary to produce a remission in the megaloblastic anaemia of patients suffering from tropical sprue. A group of 30 Puerto Rican patients with tropical sprue were given a diet containing 2,500 Calories and similar foodstuffs to those they usually consumed. Assay showed that this diet contained 50 to 75 μ g. of "free" and 1,000 to 1,500 μ g. of "bound" folic-acid-like activity. All the patients received 1 g. of iron intravenously before folic acid treatment: this did not influence the anaemia or the clinical state. The initial dose of folic acid was 25 µg.-daily by mouth; if the patient did not respond the dose was raised by 25 μ g. daily at weekly intervals until a daily dosage of 100 μ g. was reached. If 100 μ g. daily was ineffective folic acid was given parenterally, the dosage being increased by 50 μ g, daily at weekly intervals. On the basis of the haematological response the patients fell into four groups: Group 1 contained 4 patients who had previously failed to respond to antibiotic treatment but who responded to 25 μ g. daily of folic acid; Group 2 included 7 patients who responded to 25 μ g, of folic acid daily; Group 3 consisted of 8 patients who needed more than 25 μ g., up to 500 μ g., of folic acid daily; and Group 4 contained 11 patients who did not respond to doses upto 500 μ g; daily.

The response was not related to the severity of the anaemia, the degree of malabsorption, or the clinical condition of the patient. In patients who improved the response was, not surprisingly, suboptimal and megaloblasts persisted in the marrow for longer than with conventional milligramme doses. None of the patients showed improvement on a diet containing over 1 mg. of folic-acid-like activity. This folic acid is mostly in the conjugated form and may not be available because of conjugase inhibitors present in the food. The response of patients to minute doses of folic acid supports this hypothesis. The authors consider that the daily requirement of folic acid in man needs re-assessment.

M. C. G. Israels

1421. Problems in the Differentiation of the Megaloblastic Anemias

P. Heller and N. Venger. Medical Clinics of North America [Med. Clin. N. Amer.] 46, 121-138, Jan., 1962. 4 figs., bibliography.

1422. The Mechanism of Haemolysis in Favism: Researches on the Role of Non-corpuscular Factors. [In English]

F. PANIZON and C. VULLO. Acta haematologica [Acta haemat. (Basel)] 26, 337-343, 1961. 4 figs., 20 refs.

In this paper from the University of Ferrara are described the results of transfusing blood from 2 donors whose erythrocytes were known to be deficient in the enzyme glucose-6-phosphate dehydrogenase into normal recipients and into recipients recently recovered from an attack of favism. The donors' erythrocytes were labelled with radioactive chromium (51Cr) and the effect on their survival of administering fava-bean juice to the recipients on the 3rd, 4th, and 5th days following the transfusion was studied. The administration of the favabean juice was followed in the "after crisis" patients recovering from favism by an abrupt haemolysis of the transfused labelled cells; in the normal recipients, on the other hand, no increase in haemolysis was discernible.

The authors conclude that there must be extracorpuscular factors, as yet unknown, which determine the onset of favism, in addition to the intracorpuscular enzyme defect. Differences in the absorption or metabolism of fava poison could be the explanation.

J. V. Dacie

1423. "Mild Hemophilia" Affecting Both Males and Females

T. P. Bond, W. C. Levin, D. R. Celander, and M. M. Guest. New England Journal of Medicine [New Engl. J. Med.] 266, 220–223, Feb. 1, 1962. 2 figs., 16 refs.

A family is described in which a mild deficiency of antihemophilic factor (AHF, Factor VIII) is exhibited. The symptoms, clinically apparent in both males and females, did not include a vascular abnormality. The mode of transmission is uncertain. It is suggested that the transmission is sex-linked and of intermediate dominance. It may be a quantitative variant of hemophilia A (deficiency of antihemophilic factor, Factor VIII) although certain notable differences exist. Autosomal transmission is not excluded. The genetic implications are discussed.—[Authors' summary.]

1424. The Effect of Chemotherapy on Acute Leukemia in the Human

E. J. Freireich, E. A. Gehan, D. Sulman, D. R. Boggs, and E. Frei III. *Journal of Chronic Diseases [J. chron. Dis.*] 14, 593-608, Dec., 1961. 9 figs., 23 refs.

The effect of chemotherapy on acute leukaemia was studied in 178 patients admitted to the National Cancer Institute, Bethesda, Maryland, during the 5-year period 1953-8. The data, which are clearly set out in charts and diagrams, have been carefully analyzed. Repeated examination of marrow aspirates permitted classification into acute lymphocytic leukaemia (115 cases) and acute myelocytic leukaemia (63 cases); the latter group included 4 cases of monocytic leukaemia of the "histiocytic type".

The incidence of acute lymphocytic leukaemia decreased in linear fashion to the age of 20 years. The incidence of the acute myelocytic form was much more constant, but there appeared to be an excess of patients between the ages of 30 and 70 years. The best response to treatment was observed in acute lymphocytic leukaemia up to the age of 20, but the proportion of patients with complete remission fell with each 5-year age group; after the age of 20, patients with this form of leukaemia responded poorly. The proportion of patients with acute myelocytic disease who responded did not change with each age group. In patients showing complete remission the median survival time was significantly longer in those with myelocytic disease than in adults with acute lymphocytic leukaemia. The median duration of each complete remission in patients with lymphocytic disease was 5 months; patients who had one remission often had subsequent ones, but the proportion doing so was much smaller for myelocytic than for lymphocytic leukaemia, the difference being most marked in patients under 15. There was great variation, but on the whole leucopenic patients did better than those with a high leucocyte count.

In all groups the presenting symptoms had no relation to survival. In young children infection was commoner and there was less leukaemic tumour formation than in older patients. Preleukaemia was more common in myelocytic than in lymphocytic disease. In 88% death was due to haemorrhage or infection.

R. B. Thompson

1425. Myleran in the Treatment of Myelold Leukaemia (with Reference to 29 Cases Treated). (Le myleran dans le traitement des leucémies myéloldes (à propos de 29 cas traités))

J.-Olmer, P. Casanova, and — Calothy. *Théraple* [*Théraple*] 16, 751-754, Sept.-Oct., 1961 [received Jan., 1962].

In this report on the treatment with "myleran" (busulphan) of 29 cases of myeloid leukaemia seen at the Hôpital de la Conception, Marseilles, the results are compared with those in 21 cases treated by radiotherapy. The total period of observation was 6½ years, but 3 patients were lost to follow-up after 1 to 3 years. Of the remaining 26 patients treated with myleran, 2 have survived for over 6 years, 8 for 3 to 5 years, 5 for over 2 years, 7 for over one year, and 4 have been in remission

for less than one year. Of these 26 cases, 8 are still under observation and have not yet shown a remission. Those treated by radiotherapy did not fare so well. None of the 21 patients survived for 6-years, 8 were alive after 3 to 5 years, 5 after 2 years, 4 survived for over one year, and 4 for less than a year.

Primary remissions in the myleran-treated group were obtained in the majority of cases in 1 to 3 months, Strict haematological surveillance has to be maintained during treatment. The initial dose of myleran was 4 to 8 mg, four times a day, but the subsequent dosage in each case must depend upon the response. The authors conclude that myleran is a useful addition to the armamentarium of treatment of leukaemia, but stress that it must be used with discretion and care.

A. W. H. Foxell

1426. A New Chromosome Abnormality in Chronic Granulocytic Leukaemia

A. ADAMS, P. H. FITZGERALD, and F. W. GUNZ. British Medical Journal [Brit. med. J.] 2, 1474–1476, Dec. 2, 1961. 3 figs., 13 refs.

This preliminary communication from Christchurch Hospital, New Zealand, describes a patient, a man aged 34, in whom a diagnosis of chronic granulocytic myeloid leukaemia was made in 1954 and in whom the disease entered an acute phase in March, 1961. In the meantime he had been treated by splenic x-irradiation, radioactive phosphorus, and busulphan. Prednisone and mercaptopurine were used to treat the acute transformation, so that the high proportion of blast cells seen in the blood and bone marrow in March, 1961, was not found in June of that year, when both tissues showed practically normal composition.

Chromosome studies were carried out on bone marrow by direct methods without culture in March, June, and July, 1961. On all three occasions the modal chromosome number was 46, but some cells had the Philadelphia (Ph1) chromosome, some had a minute fragment, and some had both abnormalities. The minute chromosome seemed, like the Ph1, to have arisen as a consequence of a partial deletion of a small acrocentric. chromosome of the pairs 21 and 22. In addition an abnormal large chromosome, probably attributable to a translocation between chromosome No. 2 and one of the 6-12 group, was seen in some cells. All the cells with the translocation chromosome carried the Ph1. In some tetraploid cells two minute chromosomes were seen. In 3 blood cultures carried out during remission all the abnormal chromosomes seen in the bone marrow were found in blood, but in a very small proportion of cells. The genesis is discussed of both the Ph1 chromosome and of the minute chromosome found in this case. The advantages of direct examination for chromosome studies. on leukaemic material are pointed out:

[It is doubtful whether these new chromosome abnormalities are comparable with the Ph¹ chromosome as regards specificity and significance, in view of the possible effects of previous treatment and the association with acute transformation of the chronic disease.]

A. G. Baikie

Respiratory System

1427. A Contribution to the Aetiology of the Middlelobe Syndrome. (Ein Beitrag zur Ätiologie des Mittellappensyndroms)

H. G. GANGUIN and W. MEISTER. Zeitschrift für. Tuberkulose [Z. Tuberk.] 118, 1-9, 1961. 2 figs., 50 refs.

Over a period of 2 years 39 cases of the "middlelobe syndrome" were seen at the District Hospital of Cottbus, Germany, and in this paper the aetiology and pathology of the condition are discussed. Of the 16 male patients, 7 had carcinoma of the bronchus, 5 chronic non-specific inflammation, and 4 recent tuberculosis. The high proportion of cases of carcinoma in this series compared with previous series reported in the literature is attributed to the earlier diagnosis of lung cancer in recent years. The 23 female patients comprised 14 with chronic non-specific inflammation and 9 with hilar tuberculous lymphadenopathy associated with bronchitis. Thus in the female the preponderant cause of the syndrome is chronic inflammation. Pathologically there were frequently old fibrous bronchial changes, possibly of specific origin, which preceded the chronic non-specific middle-lobe inflammation. The authors note that it is important to distinguish between cases of non-specific actiology and those of tuberculous actiology before deciding upon treatment. Diagnosis is often made more difficult by overlying non-specific inflammation which masks the true underlying pathology.

D. Goldman

1428. Pulmonary Hypertrophic Osteoarthropathy H. E. Holling, R. S. Brodey, and H. C. Boland. Lancet [Lancet] 2, 1269-1274, Dec. 9, 1961. 9 figs., 17 refs.

The authors present a study of hypertrophic osteoarthropathy as seen in 5 human subjects admitted to the University of Pennsylvania Hospital, and in 7 dogs treated at the University Veterinary Hospital, Philadelphia. In the dogs, in which species this condition appears to be more common, histological studies showed an overgrowth of highly vascular connective tissue consisting of dense collagenous bundles containing many thick-walled vessels; the new bone formation was subperiosteal, with no increased vascularity of the bone. Blood flow to the affected parts of the limbs was increased in 6 dogs and in 3 patients in whom it was measured.

Various surgical procedures were found to affect the blood flow in the limbs. In one patient exploratory thoracotomy and hilar dissection was followed by diminution of the peripheral blood flow and decrease in the limb swelling; in another the bounding pulse present in the clubbed fingers was not affected by ligation of the branch of the pulmonary artery supplying the affected lobe, but disappeared as soon as the lung pedicle was severed; thereafter the blood flow in the limbs returned to normal in 5 days, the swelling subsiding some time

later. The increased limb blood flow in one dog diminished after the parietal pleura was incised, in another after periosteal rib resection, and in a third only when the pedicle of the affected lung was severed. Thoracotomy in normal dogs did not alter the peripheral blood flow unless accompanied by considerable dislocation of the mediastinum or by considerable blood loss. The intravenous injection of atropine in a dose sufficient to produce physiological effects in one dog did not affect the hyperaemia, which was reduced by section of both vagus nerves, but not by section of one alone. The increased blood flow in the affected parts of the limbs was greatly reduced by adrenaline, given intra-arterially or by iontophoresis. Cross-circulation maintained for 90 minutes between the limbs of an affected and a normal dog did not affect significantly the blood flow in either animal. Blood-gas studies in one patient and 2 of the dogs indicated that no significant veno-arterial shunt was present in the pulmonary circulation.

It is concluded that the evidence obtained in this study is against the humoral theory of causation but in favour of a neurogenic element in the pathogenesis of pulmonary osteoarthropathy, since it suggests that there is a reflex of which the afferent fibres travel from the lung in the vagus nerve. Other evidence suggests that the efferent pathway is the spinal sympathetic outflow, but this was contradicted by some single preliminary experiments in which neither unilateral lumbar sympathectomy nor the intra-arterial injection of bretylium tosylate reduced the blood flow in the affected limbs. A. Gordon Beckett

1429. Pulmonary Hyaline Membrane Formation in the Adult: a Clinicopathologic Study

T. H. CAPERS. American Journal of Medicine [Amer. J. Med.] 31, 701-710, Nov., 1961. 6 figs., 24 refs.

The occurrence of pulmonary hyaline membrane in the adult is much less well known than that in the newborn premature infant. In this study necropsy records at the Veterans Administration Hospital, Dallas, Texas, for the years 1957-9 were searched for evidence of hyaline membrane formation, while from January, 1960 onwards, sections from each lobe of both lungs of patients coming to necropsy were removed for histological examination. In this way, in the records or material from a total of 1,260 necropsies 37 cases of pulmonary hyaline membrane were found, of which 18 were severe; 4 occurred in negro patients, but no females were affected. The age range was from 31 to 80 years. For the histological studies tissues were fixed in formalin, cleared with ethyl: alcohol and chloroform, and paraffin sections 3 to 8μ in thickness were stained with haematoxylin and eosin. In selected cases Mallory stain for fibrin and Sudan black and periodic-acid-Schiff staining for fat were used. Clinical data from the records regarding blood urea and serum protein levels were examined together with notes's

of the presence or absence of aspiration of foreign bodies, pneumonitis, and treatment by tracheotomy or oxygen.

Location of the membrane was possible in 28 cases and showed that both lungs were involved in 18 cases. the left lung in 4, and the right lung in 6. In 7 cases tracheotomy had been performed before death, while 6 showed indications of aspiration, the aspirated material being amorphous. In only one of 8 patients in whom the serum protein value had been determined was this above normal (8.8 g. per 100 ml.). In 14 available cases the blood urea level ranged from 6.8 to 200 mg, per 100 ml. Of 13 patients who had received oxygen alone or oxygen with "alevaire" 5 had severe membrane formation, while 2 patients with severe membrane formation had died under anaesthesia. Among the 15 or more basic diseases from which these patients had suffered no particular or constantly recurring one was noted, except that neoplastic disease (13 cases) was associated with more severe hyaline membrane formation.

In 18 cases, mostly of pneumonia, antibiotics had been given. Histologically, the membrane formation was seen to be outside the patches of pneumonia, suggesting that coccal organisms, which produce a profibrinolysin activator, had cleared the patches and that the responsible material was fibrin. Pulmonary oedema was focal, and absent in severe cases. Of 18 patients who had received blood transfusion (in one case 192 transfusions, the membrane in this case being positive for iron) hyaline membrane formation was severe in 11, suggesting that circulatory overload was a factor. Radiation treatment had been given in 3 [but the degree of membrane formation in these cases is not mentioned].

There was no relation between administration of cortisone or ACTH and membrane formation; thus of the 18 severe cases, in only 2 had these drugs been given. Lungs affected by membrane were found to be firm, bright purplish-red in colour, with transparent pleura. They weighed from 400 to 1,200 g., being over 1 kg. in the most severe cases. Microscopically the membrane was seen to be composed of brightly eosinophilic strands of laminated material often closely applied to the alveolar walls. The triad of hyaline membrane. vascular congestion, and atelectasis occurring in premature newborn infants was not reproduced in the adult. The author considers that hyaline membrane in adults is a "transudative phenomenon rather than the result of inhalation of aspirated material or secretion of alveolar lining cells" and that it is due to a lack of pulmonary fibrinolysin.

[An interesting and instructive paper which is marred by lack of clarity in presentation.] I. M. Librach

1430. Lung Cancer among White South Africans: Report on a Further Study

G. DEAN. British Medical Journal [Brit. med. J.] 2, 1599-1605, Dec. 16, 1961. 6 refs.

The author reports from Eastern Cape Provincial Hospital, Port Elizabeth, Union of South Africa, a comparative study of lung cancer in British immigrants in the Union and in native white South Africans. Questionaries were sent to the widows of all men who had died from

this disease between 1946 and 1957 over the whole of South Africa, and also to those of a group of "control" subjects formed by taking from the register the next recorded death of a man from the same locality and within the same 5-year age group. The postal inquiry elicited only an 18% response and recourse had to be made to personal inquiries. Eventually information was obtained for 54% of the men dying from lung cancer and for 51% of the controls.

Analysis of the replies showed that in the five main cities of South Africa 93% of Union-born patients dying of lung cancer smoked cigarettes to an average number of 34 daily, compared with 85% and 26 cigarettes in the control group. Of U.K.-born cancer patients 95% smoked cigarettes, with an average of 33 a day, as against 89% and 27 a day in the controls. However, the mortality from lung cancer was, as shown in the author's previous paper (Brit. med. J., 1959, 2, 852; Abstr. Wld Med., 1960, 27, 387) 44% higher in U.K.-born men than in Union-born men. In rural areas of the Union mortality from lung cancer was low among smokers (13 deaths per 100,000 per annum), and was estimated to be only 15% of the rate in rural areas of the U.K. The length of cigarette stubs among the different groups, as also various other factors, showed no significant difference. The much higher incidence of lung cancer among U.K.-born men and in men in Union towns is attributed to atmospheric pollution, since no marked differences were found in cigarette-smoking habits and consumption. [A very interesting paper.] Arnold Pines

1431. Lung Cancer in Iceland

N. DUNGAL. Lancet [Lancet] 2, 1350, Dec. 16, 1961. 1 fig., 1 ref.

In the period 1932-40 lung cancer was found in 0.6% of necropsies on adult men and 0.3% of necropsies on adult women. Since 1950 the frequency of the disease has increased, the proportions in 1956-60 being respectively 3.0% and 2.3%. Of the 60 histologically proved cancers of the lung, 25 were adenocarcinomata and 5 were squamous, 5 undifferentiated, and 3 alveolar carcinomata. The proportion of adenocarcinomata decreased from 9 out of 14 (64%) in 1932-50 to 16 out of 36 (44%) in 1951-60. Most carcinomata occurred in Reykjavik, and the air in this town has been notably pure since 1943-4, when water from hot springs was piped into nearly every home. The sale of cigarettes was small in 1920 (less than 100 per head per annum), but since then it has increased rapidly, and in 1960 nearly 1,700 cigarettes were sold for each inhabitant aged 15 years or over.

Richard Doll

1432. Indications and Contraindications for Diaphragmocrurotomy for Pulmonary Emphysema. (Показания и противопоказания к диафрагмокруротомии при эмфиземе легких)

М. G. КUTJAKOV. Клиническая Медицина [Klin. Med. (Mosk.)] 39, 81-85, Nov., 1961. 26 refs.

The author describes from the Tomsk Medical Institute—where the procedure was devised in 1948 by Savinikh—the operation of diaphragmocrurotomy for the

relief of pulmonary emphysema. The diaphragm is divided, in the sagittal plane, from the oesophageal opening to the attachment to the xiphisternum, and the crura are divided transversely at the same level. In 36 patients with pulmonary emphysema in various stages, who are here described, the operation was performed in 31 cases under spinal anaesthesia and in 5 with local analgesia. One patient developed severe bronchopneumonia and in 4 there was partial divergence of the aponeurosis after operation. Follow-up studies to determine progress were made 4 or 5 weeks after operation, and again about a year later. In many cases vital capacity was increased by 30 to 50% and tidal expansion by 40 to 45%. The results were less good in the group of patients in whom there was loss of compensation in the pulmonary circulation. With 2 exceptions (both in this latter group) all the patients showed an increase of 9 to 12% in oxygen saturation of the arterial blood.

The indication for this operation is emphysema of the 2nd or 3rd degree with compensated circulatory failure. Absolute contraindications are decompensated right cardiac failure, well-marked diffuse pneumosclerosis, and massive costo-diaphragmatic or costo-pleural adhesions in the lower part of the thoracic cavity. Relative contraindications are purulent bronchial infections with or without bronchiectasis, bronchial asthma, advanced atherosclerosis, and advanced age.

L. Firman-Edwards

INFLAMMATORY DISEASES OF THE LUNG

1433. Bacteriological Studies in Chronic Bronchitis B. GANDEVIA and D. C. COWLING. Australasian Annals of Medicine [Aust. Ann. Med.] 10, 275-281, Nov., 1961 [received Jan., 1962]. 32 refs.

Over a period of 16 months bacteriological studies were carried out at the Royal Melbourne Hospital, Australia, on 17 patients with chronic bronchitis, who were treated with antibacterial drugs only if the clinical indications were pressing. During the last 2 months of the survey courses of antibiotics were given for various reasons. The minimum number of sputum cultures made from any patient was 3 and the maximum 36; in all, 282 specimens of sputum were investigated. All sputa were at least mildly mucopurulent, polymorphonuclear leucocytes being present on microscopical examination.

In regard to the organisms found, Haemophilus influenzae was isolated in 12 cases, all of the more severely bronchitic type, and consistently in 5 of these; Streptococcus pneumoniae was present in 7 cases (consistently in 2), and coliform bacilli in 13 patients, with consistent findings in 5. Exacerbations were seen in conjunction with the appearance of H. influenzae, Strep. pneumoniae, and coliform bacilli. In 3 cases exacerbations, in which coliform bacilli appeared as likely pathogens, followed oral penicillin therapy. In addition a variety of organisms usually not regarded as potential pathogens, such as β -haemolytic streptococci, Proteus vulgaris, Bact. alkaligenes, and a chromobacterium, were isolated. The authors consider that neither these miscellaneous organ-

isms nor, in particular, coliform bacilli can be excluded as pathogens in patients with a damaged mucous membrane of the lower respiratory tract, and that such organisms, if less susceptible to antibacterial drugs, may assume greater significance after the administration of antibiotics.

K. ZInnemann

1434. Prophylactic Use of Influenza Vaccine in Patients with Chronic Bronchitis: a Pilot Trial

C. H. L. Howells and L. E. Tyler. *Lancet* [Lancet] 2, 1428-1432, Dec. 30, 1961. 1 fig., 22 refs.

A trial of the effectiveness of the influenza vaccine "flubron" in reducing the number and severity of acute exacerbations in patients with mild or moderately severe chronic bronchitis was carried out in a Wolverhampton general practice. Of the 55 patients taking part, 26 were allotted at random to a treatment group and received one injection of flubron vaccine (A.A2 Asian-Formosa 7000, B. England 5000), while the remaining 29 received an injection of saline solution as a control. The two groups were similarly constituted as regards age, sex, and severity of bronchitis. During the observation period, which extended from December, 1960, to March, 1961, there were 10 exacerbations of bronchitis in 10 patients in the vaccinated group and 24 exacerbations in 20 patients in the control group. Most of the exacerbations in the treated group occurred in the first 3 weeks after vaccination, during which the effect of the vaccine may not yet have been established. If this period is excluded, then during the remainder of the period of observation there was only one exacerbation in the vaccine-treated group, which was not associated with a positive complement-fixation reaction to any virus. In the same period there were 12 exacerbations in the control group, 7 of which were associated with positive complement-fixation reactions to viruses included in the vaccine. Exacerbations were identified both by clinical observation and by the recording of a significant fall in respiratory capacity as measured by the Wright peak-flow meter.

The authors consider that the prophylactic use of influenza vaccine in this trial greatly reduced the incidence of exacerbations, and that the vaccine will have a major part to play in the management of chronic bronchitis.

Bernard Isaacs

1435. Mucoviscidosis and Adult Chronic Bronchitis: their Possible Relationship

D. Muir, J. Batten, and G. Simon. *Lancet* [Lancet] 1, 181-183, Jan. 27, 1962. 15 refs.

At the Brompton Hospital, London, the authors have determined by means of the finger-print test the chloride content of the sweat of 100 patients with chronic bronchitis, 42 with other chronic, non-tuberculous, lung disease, and 25 control patients. Of the 100 with chronic bronchitis 63 showed radiological evidence of emphysema and all but 13 had reduced peak expiratory flow rates. No difference was found in the distribution of the results of the finger print tests in the three groups of subjects. A further study of 31 of the bronchitic patients by chemical analysis of the sweat revealed that in no case was the sweat chloride concentration greater than

70 mEq. per litre. The authors conclude that mucoviscidosis in the homozygous state cannot be implicated as a cause of chronic bronchitis. They are now further investigating the possibility that heterozygotes (that is, parents of patients with undoubted mucoviscidosis) may show a higher than normal incidence of chronic bronchitis.

C. M. Fletcher

1436. Sweat Sodium Levels in Normal Subjects, in Pibrocystic Patients and their Relatives, and in Chronic Bronchitic Patients

T. McKendrick. Lancet [Lancet] 1, 183-186, Jan. 27, 1962. 2 figs., 11 refs.

The sweat sodium concentration, after the induction of localized sweating by the iontophoresis of pilocarpine nitrate, was studied at the Hospital for Sick Children, Great Ormond Street, London, in 288 normal subjects aged between 0 and 85 years, in 100 patients aged from 0 to 16 years with fibrocystic disease (mucoviscidosis), in 57 of their siblings and 112 of their parents, as well as in 57 adult patients with chronic bronchitis seen elsewhere.

In the normal subjects there was a gradual rise in the mean sweat sodium concentration with age, but in only 3 (1.6%) of 191 of these subjects who were under the age of 20 was the value over 70 mEq. per litre, whereas 95 of the 100 fibrocystic children had levels greater than this. The mean value in siblings of the fibrocystic patients was significantly higher than that in the normal children between the ages of 5 and 14 years, but there was considerable overlap in these two groups and only 4 out of 57 siblings had values greater than 70 mEq. per litre. The mean value for parents of fibrocystic children also differed significantly from that in normal subjects of similar age, 18% of them showing sweat concentrations above 70 mEq. per litre. The mean level in the adult chronic bronchitic patients was just significantly higher than that in the normal subjects, but there was great overlap; 17% of them showed a figure of 70 mEq. per litre or greater. The author comments that the wide variation of results. both in single subjects and within groups of similar subjects, limits the value of the test, which he therefore considers is useful "only for confirming the diagnosis of fibrocystic disease".

[The author does not comment on the significance of the mean differences between the normal subjects, siblings, and parents of fibrocystic patients on the one hand and the patients with chronic bronchitis on the other; nor does he say whether the subjects with a higher sweat sodium level had respiratory symptoms. This test may be of more diagnostic value than the author admits.]

C. M. Fletcher

1437. Chronic Bronchitis and Mucoviscidosis

E. Bernard, L. Israel, and M. M. Debris. American Review of Respiratory Diseases [Amer. Rev. resp. Dis.] 85, 22-24, Jan., 1962. 11 refs.

The authors have carried out sweat chloride analyses on 75 patients with chronic bronchitis, 51 with pulmonary tuberculosis, 23 with asthma, and 26 with other pulmonary conditions, all of whom were tested on admission to

the Hôpital Laennec, Paris. They consider that any value of sweat chloride content over 50 mEq. per litre indicates abnormality; on this criterion 27 (36%) of the chronic bronchitics showed abnormal values, while only one of the other subjects had a level exceeding 50 mEq. per litre. The authors conclude that a large proportion of cases of chronic bronchitis are attributable to mucoviscidosis, and quote reports by other workers who have found similar proportions of abnormal results in patients with chronic bronchitis.

[The discrepancy between this report and those of Muir et'al. and McKendrick (see Abstracts 1435 and 1436) is difficult to explain, but may lie in the fact that all the patients in this study were in-patients and therefore presumably had recently been acutely ill. It is stated that one of the chronic bronchitics was in fact the mother of a child with mucoviscidosis, but no details of the family history of the other chronic bronchitics are given. In this connexion Karlish et al. (Lancet, 1962, 1, 429) suggest that selection of patients is probably the basis of the discrepancies between the results of this test as reported by different authors.]

1438. Hemophilus influenzae in Adult Bronchopulmonary Infection

T. A. KEITH III and A. W. Schreiner. Annals of Internal Medicine. [Ann. intern. Med.] 56, 27-38, Jan., 1962. 4 figs., 24 refs.

Five cases of pneumonia or severe, acute purulent bronchitis due to Haemophilus influenzae seen within 15 months at the Veterans Administration Hospital, Cincinnati, Ohio, are described in considerable detail. The patients' ages ranged from 42 to 64 years, and 4 of them had been suffering from mild chronic respiratory disorders—such as asthma, or wheeziness following previous chest infections or in conjunction with heavy smoking. for some years preceding the pneumonic episodes. The fifth patient developed pneumonia as a complication of an acute infero-lateral myocardial infarction. Four of the patients were seen during January and February, 1960, when there was a peak incidence of H. influenzae in sputum cultured at the hospital. The conditions were regarded as having been primarily due to H. Influenzae infection because: (1) there was x-ray evidence of pneumonia or bronchitis; (2) there was an abundant growth of H. influenzae in sputum cultures: (3) the patient had not received streptomycin, tetracyclines, sulphonamides, or chloramphenicol during the previous month; and (4) a favourable clinical response followed the administration of one or more of these drugs.

The paper makes two points in particular: (1) acute *H. influenzae* infections, contrary to common belief, occur in adults, and particularly in patients with chronic respiratory disease; and (2) in such patients adequate bacteriological technique leads to correct diagnosis and may be life-saving.

[There is no indication whether the *H. influenzae* strains isolated belonged to the capsulated types with high virulence, or to the non-capsulated variety predominantly found in large numbers in chronic infections of the upper and lower respiratory tract.]

K. Zinnemann

Urogenital System

1439. Pathogenesis of Uremic Acidosis as Indicated by Urinary Acidification on a Controlled Diet

A. P. Brigos, W. H. Waugh, W. S. Harms, and T. Findley. *Metabolism: Clinical and Experimental [Metabolism]* 10, 749–762, Oct., 1961. 49 refs.

In this study reported from the Medical College of Georgia, Augusta, 6 patients with chronic nephritis and 7 convalescent patients without cardiac or renal disease were given 60 millimols of dibasic ammonium monohydrogen phosphate in 4 divided doses daily for 3 days and all received the same test diet on the third day. Thereafter a 10-hour overnight collection of urine was made, followed by blood sampling for chemical analysis. The priming with phosphate was intended to increase the plasma inorganic phosphate concentration in the nephritic subjects to levels at which metabolic equilibrium with the phosphate intake on the day of the test diet could be maintained.

It was found that the urinary excretion of phosphate. sulphate, and chloride was similar in the two groups. The mean titratable acidity of the urine was 15.5 mEq. for the normal subjects and 17-0 mEq. for the nephritic patients, while the corresponding urinary pH levels were 5.5 and 4.9; mean urinary total fixed anion excretions were 79.5 and 79.0 mEq. respectively, and the mean total fixed cation excretions 42 and 48 mEq. respectively (31.0 and 32.5 mEq. for sodium and 11.0 and 15.5 mEq. for potassium). This study therefore produced no evidence of a serious tubular defect in the formation of titratable acid. The nephritic group excreted a larger volume of urine than the control group and their excretion of ammonia was about 60% of that of the controls. The authors emphasize the importance of less net urinary acidification and small net loss of fixed cation (largely potassium) in the urine of nephritics and they consider that retention of excess fixed anions is the dominant factor in the pathogenesis of uraemia. K. G. Lowe

1440. Radiation Nephritis: a Long-term Study of 54.

R. W. Luxton. Lancet [Lancet] 2, 1221-1224, Dec. 2, 1961. 3 figs., 4 refs.

The long-term results in 54 patients treated by abdominal irradiation for malignant testicular or ovarian tumours at the Christie Hospital, Manchester, and who later developed radiation nephritis are reported after 13 years' observation. In 20 cases acute radiation nephritis developed 6 to 13 months afterwards, always with hypertension. Six out of 8 of these patients with malignant hypertension died; another 3 patients died from chronic renal failure. Nine patients are well; though with chronic nephritis. Another group of 10 patients have also developed chronic nephritis, 3 dying of uraemia after a few years. Six others had benign hypertension, one dying from a malignant phase and 2 from congestive

heart failure. Thirteen other patients had symptomless proteinuria with a latent nephritis. Among the 54 patients, 15 developed either early (8) or late (7) malignant hypertension.

Arnold Pines

1441. The Intestinal Absorption of Calcium in Nephritis with Renal Insufficiency. (L'absorption intestinale du calcium dans les néphrites avec insuffisance rénale)

A. LICHTWITZ, S. DE SEZE, R. PARLIER, D. HIOCO, and P. BORDIER. *Presse médicale* [*Presse méd.*] 69, 2054–2056, Nov. 4, 1961. 1 fig., bibliography.

At the Hopital Lariboisière, Paris, 10 patients with various types of renal disease were investigated for intes-, tinal calcium absorption. In patients with Bright's disease and no bony lesions an increase in faecal calcium excretion was found. A comparison of the results of calcium balance studies after administration of calciferol, intravenous calcium, and radioactive calcium seemed to indicate that the increase in faecal calcium excretion in these cases was due to a reduced ability of the intestinal cells to absorb exogenous calcium. It is thought probable that this intestinal defect is the cause of the bony lesions and parathyroid hyperplasia found in nephritis with chronic renal insufficiency rather than any increase in the intestinal excretion of calcium removed from the G. W. Csonka skeleton by osteolysis.

1442. Pulmonary Oedema in Acute Glomerulonephritis J. G. WILSON. Archives of Disease in Childhood [Arch Dis. Childh.] 36, 661–668, Dec., 1961. 4 figs., 24 refs.

At the Children's Hospital, Adelaide, South Australia, 3 children died within 24 hours of admission with a clinical picture of acute cardiac failure and pulmonary oedema. No treatment had any effect. Owing to the desperate nature of the illness no urine was obtained for testing during life and few investigations were possible. At necropsy, however, the uniform finding was a picture of acute nephritis with diffuse glomerular changes which included avascularity, cellular proliferation, leucocytic infiltration, and the formation of hyaline thrombi in the kidneys. The tubules were practically normal. The pulmonary oedema was considered to be secondary to the renal disease.

The actiology of the pulmonary ocdema is discussed in detail, without any definite conclusion being arrived at which would be applicable to these cases, possibly because of the paucity of investigations. The failure of all forms of treatment, including positive-pressure respiration, is commented upon:

John Lorber

1443. The Mechanism of the Renal Excretion of Oxalate in the Dog

W. R. CATTELL, A. G. SPENCER, G. W. TAYLOR, and R. W. E. WATTS. Clinical Science [Clin. Sci.] 22, 43-51, Feb., 1962. 4 figs., 17 refs.

Endocrinology

1444. Differences in the Response of Euthyroid and Hyperthyroid Patients to Thyro-inhibitory Substances M. L. MITCHELL, M. E. O'ROURKE, and A. B. HARDEN, Journal of Clinical Endocrinology and Metabolism [J. clin. Endocr.] 21, 1566-1571, Dec. 1961. 4 figs., 7 refs.

The authors studied the thyroidal uptake of radioactive iodine (131I) before and after the administration of potassium thiocyanate or thiourea in groups of healthy controls and in patients with non-toxic goitre or with unequivocal thyrotoxicosis.

Both substances markedly reduced the uptake of ¹³⁴I in the euthyroid subjects, but they exerted a much smaller effect in the thyrotoxic patients. The overlap of the uptakes after administration of potassium thiocyanate in the euthyroid and thyrotoxic groups appeared to be due to differences in the blood levels of thiocyanate. The inhibitory effect of thiocyanate varied directly with its blood concentration, the thyrotoxic tending to have lower serum levels. There was virtually no such overlap of uptakes after the administration of thiourea. Patterns similar to those observed in the thyrotoxic patients had been obtained previously in healthy subjects given thyrotrophin.

The authors speculate whether these inhibitory materials are metabolized in the thyrotoxic gland at an accelerated rate, or whether the rapid turnover of iodine in the hyperfunctioning gland may compensate for the reduction in function produced by the inhibitory substances.

A. Gordon Beckett

PITUITARY GLAND

1445. Partial Pituitary Ablation by Needle Implantation of Gold-198 Seeds for Acromegaly and Cushing's Disease G. F. Joplin, R. Fraser, R. Steiner, J. Laws, and E. Jones. *Lancet* [Lancet] 2, 1277–1281, Dec. 9, 1961. 5 figs., 17 refs.

The preliminary results obtained in 18 patients with acromegaly and 6 with Cushing's disease in whom radioactive gold (189Au) was implanted in needles to effect partial pituitary ablation are reported in this paper from the Postgraduate Medical School, Hammersmith Hospital, London. Full details of the technique are given together with the results of clinical and biochemical assessment of the patients' condition before and after treatment.

Of the 18 patients with acromegaly 7 had previously been given external irradiation without regression of the clinical manifestations of the disease. Almost all the 18 acromegalics had symptomatic relief together with diminution in the signs of the disease in response to treatment with ¹⁸⁹Au, this symptomatic relief being evident within the first week. Tests of carbohydrate metabolism showed changes in most cases, and in one of the 3 dia-

betics who had required insulin there was a normal oral glucose tolerance curve together with a normal response to a prednisone glycosuria test; in the remaining 2 diabetics good clinical control was achieved with either diet or minimal dosage of insulin.

In 4 of the 6 patients with Cushing's disease there was a striking but incomplete remission; the remaining 2 showed no improvement by any criteria. In the 4 patients with remission there was improvement not only in the clinical manifestations but also in the urinary excretion of steroid.

The complications in this series of 24 patients were minimal; in particular there was no loss of cerebrospinal fluid or cranial-nerve damage. Visual fields, which were carefully plotted in all cases, remained unchanged and only one patient required subsequent replacement therapy. In one patient with acromegaly pituitary infection developed. The authors consider that there were signs of such infection in 4 cases; in 3-the signs subsided rapidly with chemotherapy, but in the fourth the administration of antibiotics was delayed, resulting in meningitis, which proved fatal.

It is concluded that the dosage of irradiation used was probably a little too low and that in the future a combination of ¹⁹⁸Au and ⁹⁰Yt should prove superior. The authors consider that the results in the cases of Cushing's disease were more encouraging and they do not intend to modify the procedure in these cases.

J. Warwick Buckler

1446. A Method of Determining the Pitultary Reserve of Thyroid Stimulating Hormone. (Eine Methode zum Nachweis der hypophysären TSH-Reserve)
H. STUDER and F. Wyss. Schweizerlsche medizinische Wochenschrift [Schweiz. med. Wschr.] 91, 1536–1539, Dec. 16, 1961. 4 figs., 7 refs.

It is well known that if the production of hormone in the thyroid gland is blocked by antithyroid substances the amount of thyroxine in the blood is diminished. The, "braking" effect of circulating thyroid hormone on. secretion of thyroid stimulating hormone (T.S.H.) is removed and increased output of T.S.H. follows: this is shown morphologically by hyperplasia of thyroid tissueand biochemically by increased synthesis of hormone in the thyroid gland. This type of "feed-back-" mechanism is well recognized. After hypophysectomy there is no further secretion of T.S.H. and therefore no evidence of activation of thyroid tissue after administration of antithyroid substances. The same holds true when an endogenous thyroxine deficit is treated by giving thyroxine. On the basis of these considerations the following method for determining the pituitary reserve of T.S.H. was devised by the authors, working at the Inselspital. Berne. In this test the uptake of ¹³¹I is assessed before giving "neo-mercazole" (carbimazole) and 36 hours after the last dose, interim readings being taken after

2, 8, and 24 hours. Carbimazole was given in a dosage of 15 mg. four times a day (total 60 mg.) for at least 5 days in the case of adults. The increased thyroid production due to the greater amount of circulating T.S.H. (normal rebound effect) will be the more marked, the longer neo-mercazole is given. Patients with impaired pituitary function—for example, in acromegaly—will show a negative rebound effect by exhibiting lower thyroid production after the block than before it. Of 30 patients investigated, only 8 with normal pituitary function and 7 with abnormal pituitary function are discussed in detail.

The test appears to the authors to be a sensitive and useful one, especially in the case of a tumour encroaching upon the pituitary gland and of other lesions at the base of the brain. There are, however, pitfalls, which have to be avoided; one of these is retarded pituitary function which may simulate a negative rebound effect, which occurred in one of the authors' patients who was suffering from obesity.

[The interesting observation made in 2 women with malignant exophthalmos who were clinically euthyroid but showed a negative rebound effect requires explanation.]

V. C. Medvei

PARATHYROID GLANDS

1447. Prevalence of Parathyroid Insufficiency after Thyroidectomy

R. H. DAVIS, P. FOURMAN, and J. W. G. SMITH. *Lancet* [Lancet] 2, 1432–1435, Dec. 30, 1961. 2 figs., 20 refs.

The authors report from the Royal Infirmary, Cardiff, a study of the incidence of partial parathyroid insufficiency after thyroidectomy in 82 unselected patients in two defined populations, a strictly selected series of 80 patients who had not been operated on serving as controls.

Of the 82 patients who had undergone thyroidectomy only one subsequently had tetany and in only 2 was the plasma calcium level below the lower limit found in the controls. The mean plasma calcium level in the thyroidectomized group (9.52 mg. per 100 ml.) was lower than that in the control group (9.72 mg. per 100 ml.). There was, however, a much greater spread in the levels of the plasma calcium in the thyroidectomized patients than in the controls; 34% of the former group had a plasma calcium level below 9.3 mg. per 100 ml. as compared with 10% of the control group. There was no correlation between these low levels and the plasma protein or plasma phosphorus levels.

A calcium deprivation test (low-calcium diet with administration of sodium phytate) was carried out on 19 patients, the response being considered abnormal if the plasma calcium level fell below 8.5 mg. per 100 ml. The patient who had had tetany gave an abnormal response, as did 10 out of 11 without a history of tetany but with some of the vague symptoms which, in the authors' view, are attributable to hypoparathyroidism. The response to the test was normal in 7 patients without such symptoms in the group with the lower plasma

calcium levels. Symptoms were often relieved by the administration of calcium citrate.

The authors conclude that although gross hypoparathyroidism may not be evident after thyroidectomy subclinical forms are common and in this series probably 24% of the patients had some degree of insufficiency. They consider that this insufficiency is due to the small endarterial supply of the parathyroid glands from the inferior thyroid artery, and that damage results from surgical haemostasis.

J. Warwick Buckler

1448. Peptic Ulcer in Primary Hyperparathyroldism: an Analysis of Fifty-two Cases

W. T. WILDER, B. FRAME, and W. S. HAUBRICH. Annals of Internal Medicine [Ann. intern. Med.] 55, 885-893, Dec., 1961. Bibliography.

The authors report the finding of peptic ulcer in association with primary hyperparathyroidism in 7 out of 10 patients seen at the Henry Ford Hospital, Detroit, between 1958 and 1960 and analyse these together with 45 similar cases reported in the literature. A gastric ulcer was diagnosed in 9 patients, duodenal ulcer in 41, while 2 had both a gastric and a duodenal ulcer. Frequently the ulcer symptoms had been present for 10 to 20 years. In 23 cases the ulcer symptoms, improved after removal of the parathyroid glands. Of 48 cases in which the sex was stated 31 were in males and 17 in females, a ratio of nearly 2:1, compared with 4:1 for all cases of peptic ulcer, suggesting that there is an increased incidence of ulcer in females with hyperparathyroidism. The peak age incidence (26 cases) was in the 5th decade; there was no difference in the age of those patients with hyperparathyroidism and ulcer and those with hyperparathyroidism without ulcer. Histological studies revealed a single adenoma in 36 patients, while 12 patients exhibited parathyroid hyperplasia, the latter being usually of the "clear-cell" type. The authors discuss fully the relationship between peptic ulcer and hyperparathyroid-I. McLean Baird

DIABETES MELLITUS

1449. The Long-term Use of Sulphonylureas in Diabetes Mellitus

J. M. Stowers and P. D. Bewsher. Lancet [Lancet] 1, 122-125, Jan. 20, 1962. 3 figs., 8 refs.

In this paper from the University of St. Andrews, Queen's College, Dundee, the results are reported of the long-term treatment of diabetic patients with sulphonylureas, 267 diabetics being given chlorpropamide and 66 tolbutamide. Of the 267 patients receiving chlorpropamide 72% were judged to be perfectly controlled—that is, the random blood sugar level was below 150 mg. per 100 ml.; of the 66 patients receiving tolbutamide 58% were perfectly controlled. In 24 patients on long-term treatment with chlorpropamide diabetic complications progressed, even though 16 of these patients were perfectly controlled. Only 4 patients in the chlorpropamide group showed improvement in complications. The toxic effects of the two drugs included rash, dyspep-

The Rheumatic Diseases

1453. A Comparison of the Uricosuric Agents Used in the Treatment of Gout. [In English]

G. D. KERSLEY. A.I.R. Archives of Interamerican Rheumatology [A.I.R. Arch. interamer. Rheum. (Rio de J.)] 4, 311-319, Sept., 1961 [received Feb., 1962]. 2 figs., 4 refs.

The author has made a controlled comparison of the chief uricosuric drugs in present-day use, noting their toxicity and the precautions which should be taken when using them. Fifty cases of typical gout were treated with 4 uricosuric agents—sulphinpyrazone ("anturan"), zoxazolamine, ethebenezid ("urelim"), and probenecid ("benemid")—and observed for 3 years. It was found that ethebenezid, 1.5 g. daily, gave better results than probenecid in the same dosage, but was less effective than sulphinpyrazone in a dosage of 800 mg. per day. Zoxazolamine, 1.5 g. daily, was as effective as sulphinpyrazone, 400 mg. daily. With both sulphinpyrazone and zoxazolamine there was a tendency to exacerbation of attacks during the first 6 weeks of treatment, but after that there was a marked decrease in the rate and severity of attacks and in the size of tophi.

The author states that as a result of these studies he has adopted the following plan of treatment of gout where attacks are recurrent, the plasma uric acid level is persistently raised, or there is tophus formation. For the first 3 weeks the patient receives 400 mg. of sulphin-pyrazone together with 1.5 mg. of colchicine daily, in addition to extra fluids and a small dose of alkali. The dose of sulphinpyrazone is then increased to 600 or 800 mg., and after 6 weeks' treatment the colchicine is stopped if there have been no acute exacerbations. If a severe attack occurs 600 to 800 mg. of phenylbutazone is administered for 2 days only. Should analgesics be also required paracetamol is given. W. S. C. Copeman

ACUTE RHEUMATISM

1454. The Latent Period before the Onset of Acute Rheumatic Fever

C. H. RAMMELKAMP JR. and B. L. STOLZER. Yale Journal of Biology and Medicine [Yale J. Biol. Med.] 34, 386–398, Dec., 1961–Feb., 1962. 1 fig., 12 refs.

A group of airmen suffering from rheumatic fever were studied at the Francis E. Warren Air Force Base, Wyoming, to determine the natural history of the latent period between the initial streptococcal infection and the onset of the rheumatic symptoms. Analysis was limited to the 251 patients for whom the dates of onset of the tonsillitis and of the rheumatic fever were known; and these were observed throughout their illness. In 113 of these patients an infection by a single type of streptococcus occurred, but no specific therapy was given. In this group the mean latent period was 18 6 days (from the first day of the streptococcal illness to the onset of the

rheumatic symptoms). The majority were thought to have experienced a single preceding streptococcal infection, but a few who had a very short latent period may have had a preceding, clinically inapparent infection. In favour of this theory was the observation of high antistreptolysin-O titres in the acute-phase serum of some such patients. At the other extreme, patients who had a latent period of over 35 days were considered to have developed a second clinically inapparent streptococcal infection which was not detected by the techniques employed. The length of the latent period did not appear to be related to the type of streptococcus responsible for the infection, nor was the latent period shortened in the 21 patients with second or recurrent attacks of rheumatic fever. The value of penicillin treatment of streptococcal infections in the prevention of rheumatic fever is reaffirmed, even if it is started as long as 4 weeks after the onset. John Lorber

1455. Long-term Effects of ACTH and Cortisone Therapy in Rhematic Fever: Cardiologic Observations on Patients 5 to 8 Years after Hormone Therapy in a Controlled Study S. FRIEDMAN, T. N. HARRIS, and J. L. CADDELL. Journal of Pediatrics [J. Pediat.] 60, 55-61, Jan., 1962. 12 refs.

A number of controlled studies of ACTH and cortisone (or its derivatives) in the treatment of acute rheumatic fever have been reported since 1948, the control patients receiving either salicylate therapy or merely symptomatic treatment. No significant difference has been observed in the residual cardiac damage within a few weeks or months of the cessation of treatment. What is perhaps of more interest is an evaluation of the cardiological findings in hormone-treated and control patients some years after therapy. Such a report has been presented by a combined United Kingdom-United States group of workers covering a study in which approximately 500 patients, including controls, were followed up for an average of 5 years. Here the controls were treated with salicylates and again no significant difference was found in the incidence or severity of cardiac residua.

Between 1950 and 1953, 100 consecutive episodes of rheumatic fever in 91 patients, with or without carditis, were treated at the Children's Hospital of Philadelphia. These patients were divided into 3 groups, receiving cortisone, ACTH, and symptomatic treatment respectively. On their discharge from hospital there was no essential difference in the cardiac status of the children in the several treatment groups.

In the present communication the results of a reexamination 4½ to 8½ years later of 65 of these 91 patients are presented. In the original study (*Pediatrics*, 1956, 17, 11; *Abstr. Wld Med.*, 1956, 20, 139) the average duration of treatment was 3½ weeks; the dosage of ACTH ranged from 40 to 100 mg, and that of cortisone from sia, jaundice, anaemia, and hypoglycaemia. The lastnamed complication occurred in 6% of the tolbutamide group and 7.1% of the chlorpropamide group, and was considered by the authors to be an effect of overdosage rather than a toxic effect.

The maximum dosage of chlorpropamide was 500 mg. daily while that of tolbutamide was 500 mg. 3 times a day. About 8% of the patients taking each drug failed to respond in the first month of treatment. The possible causes of secondary failure, which the authors found was more likely during the first year of treatment than later, are discussed. Long duration of diabetes appeared to be a factor, but there was little correlation with the initial blood sugar level or the initial weight of the patient.

1. McLean Baird

1450. The Lente Insulin Triad; with Emphasis on the Use of "Lente Combinations"

F. W. WHITEHOUSE, W. L. LOWRIE, E. REDFERN, and J. B. BRYAN. Annals of Internal Medicine [Ann. intern. Med.] 55, 894-902, Dec., 1961. 8 refs.

The authors describe their experience at the Henry Ford Hospital, Detroit, with the three types of "lente" insulin: (1) ultralente having a maximum action 18 to 24 hours after injection, (2) lente insulin, with maximum action after 8 to 14 hours, and (3) semilente, a rapid acting insulin exerting maximum effect at 2 to 4 hours. Of 65 diabetic patients dependent on insulin 42 received a combination of the lente and ultralente forms; this proved very useful in those patients requiring more than one injection daily, and also if there was fasting hyperglycaemia or mid-afternoon hypoglycaemia. A further 18 patients received a combination of the semilente and lente insulins, and 5 a combination of the ultralente and semilente preparations. The authors suggest that semilente should be used with lente insulin when greater hypoglycaemic activity during the day is needed. Only minor disadvantages were experienced, and it is noted that these preparations avoid the drawbacks of insulins with added foreign protein. I. McLean Baird

1451. The Use of Saliuretics in Diabetes. (Die Verwendung von Saluretika bei Diabetikern)
R. P. Königstein and G. Mähr. Wiener medizinische Wochenschrift [Wien. med. Wschr.] 112, 82-84, Jan. 27, 1962. 2 figs., 14 refs.

Writing from the metabolic unit of Lainz Hospital, Vienna, the authors discuss the indications for saliuretic therapy in diabetes and its possible effects on the degree of control of the disease. The dangers of such drugg were illustrated by the case of a previously well controlled diabetic patients, an obese female aged 53, in whom a 5-day course of 50 mg. of hydrochlorothiazide, administered with the aim of reducing the patient's weight before a gynaecological operation, resulted in the development of diabetic pre-coma, which however responded to treatment. With due precautions, therefore, 15 diabetic patients with oedema of either cardiac aetiology or due to diabetic angiopathy and one without oedema were given a 4- or 5-day course of bezylhydrofiumethiazide, 10 mg. daily. All the patients had previously been well

controlled, 9 with insulin, one with "invenol" (carbutamide), and 6 by diet alone.

The diuretic response, shown to be due to sodium loss, was uniformly good, being on the average 2 litres on the first day, 1.6 litre on the second day, and then gradually diminishing. In 2 patients with hepatic cirrhosis there was a temporary hypokalaemia of 3.85 and 3.92 mEq. per litre respectively. In 4 patients, one of whom developed glycosuria, a definite decrease in glucose tolerance was noted; this, however, reverted to its previous state without changing the diabetic regimen on withdrawal of flumethiazide. The authors conclude that saliuretics can be given to diabetic patients provided strict control of the diabetic state is exercised.

H. F. Reichenfeld

1452. Cycloheptolamide and Acetohexamide in Therapy of Diabetes Mellitus

M. C. BALODIMOS, W. H. STIMSON, D. C. TANNER, J. A. REID, and R. H. WILLIAMS. *Metabolism: Clinical and Experimental [Metabolism]* 10, 1063–1073, Dec., 1961 [received Feb., 1962]. 4 figs., 20 refs.

The value in the treatment of diabetes of cycloheptolamide and of acetohexamide, which are structurally related to tolbutamide, was assessed over periods up to 10 months in patients seen at affiliated hospitals of the University of Washington School of Medicine, Seattle.

Cycloheptolamide was given to 71 patients who seemed likely to respond to a sulphonylurea. Control was good in 37 (fasting blood sugar level <130 mg. per 100 ml. and postprandial level <150 mg. per 100 ml.), fair in 15. and poor in 19. The dosage ranged from 100 mg. to 600 mg. (average 315 mg.) daily. In 55 patients the degree of control was compared with that previously obtained in response to tolbutamide or chlorpropamide; in 41 cases it was the same, in 7 it was better, and in 7 it was worse. None of the patients in whom the diabetes was poorly controlled by the other sulphonylureas obtained good control with cycloheptolamide. The drug was discontinued in 6 cases because of side-effects (indigestion in 2, hypoglycaemia in 2, pruritus in one, and transient neuropathy in one). Other side-effects were not troublesome. "Bromsulphalein" retention was not affected, and changes in weight showed no consistent trend.

Acetohexamide was given for an average period of 10 weeks to 27 patients, in most of whom there had been a good or fair response to cycloheptolamide. Good control was achieved in 13 patients with acetohexamide alone and in 3 others with a combination of acetohexamide and phenformin; in 8 control was fair or peor, while in the remaining 3 satisfactory evaluation was not possible. The average daily dose in patients whose diabetes was well controlled was 672 mg. In general, the control was equal to or less complete than that obtained with cycloheptolamide or other sulphonylureas. Side-effects in 3 patients (nausea in one, anorexia, nausea, and vertigo in one, and hypoglycaemia in one) led to cessation of acetohexamide therapy.

It is concluded that cycloheptolamide and acetohexamide are effective and safe hypoglycaemic agents but that they offer no advantages over tolbutamide and chlorpropamide.

T. B. Begz 120 to 300 mg., daily. Of the 65 patients now reviewed, 6 had died: 2 during the original study, and 4 subsequently. Approximately 60% of the patients in each of the treatment categories had received prophylactic therapy since the acute episode.

The general conclusion is that there had been no reduction in the incidence or severity of cardiac manifestations in the hormone-treated patients compared with those given only symptomatic treatment. The criteria were: (1) changes in the number of cardiac murmurs; (2) extent of transmission of murmurs of mitral insufficiency; (3) number of recurrences of acute rheumatic fever; and (4) incidence of congestive heart failure. The figures show evidence of a definite influence of antistreptococcal prophylaxis on the percentage of recurrences; but it had apparently no beneficial effect on the ultimate incidence of cardiac residua.

Kenneth Stone

1456. The Clinical Picture of Adult Rheumatic Carditis. [In English]

M. VIRKKUNEN, H. LAITINEN, and T. SEPPÄLÄ. Acta rheumatologica Scandinavica [Acta rheum. scand.] 7, 191–200, 1961. 2 figs., 13 refs.

The clinical picture of adult rheumatic carditis was studied in 96 patients seen at Kivelä Hospital, Helsinki, who were considered to be free from the disease before admission. All the patients were over 15 years of age; 19 were under 20 years and the oldest was 57. Pericardial signs predominated in 6 patients only; myocarditis was the main feature in 68 and endocarditis in 22. A total of 55 patients were followed up for periods of 1 to 12 years (average 8 years); the remainder were patients of low social status who moved frequently. Only 3 relapses were recorded in these 55 cases. In one patient progressive heart disease and decompensation developed. Mild persisting signs of carditis were observed in 23 patients, while 14 had a murmur suggesting mitral valve disease although radiological changes confirming this were absent-the "mitral regurgitation" stage. In several cases a murmur, both systolic and diastolic, suggesting valvulitis, which was heard during convalescence, had disappeared at the time of follow-up examination; as the authors note, other workers have suggested that "valvulitis is frequently over-diagnosed".

The present series were studied during a period when penicillin prophylaxis was not available or was inadequate; the results are considered to provide evidence in support of the view that adult rheumatic carditis is today a relatively mild disease.

B. E. W. Mace

1457. Hydroxyzine in the Treatment of Rheumatic Chorea in Children

1 2 1

A. EL-GHOLMI and Y. W. ABOUL-DAHAB. Archives of Pediatrics [Arch. Pediat.] 78, 478-482, Dec., 1961. 9 refs.

The authors, who report from Ein Shams Faculty of Medicine, Cairo, have compared the effect of hydroxyzine with phenobarbitone in the treatment of rheumatic chorea. After being observed for 2 or 3 days to assess the severity of the disorder, cases were divided into 2 groups, 12 of them receiving hydroxyzine, 50 mg. thrice daily, and 10 being given phenobarbitone, 0.03 g. twice

- daily for children of 8 years or under and thrice daily for older children. (Three of the cases included among the latter group had been readmitted following a relapse.)

Of the cases treated with hydroxyzine, improvement was seen in 7 by the 8th day and in 11 in 2 weeks, while 6 had recovered completely within 3 weeks. In 2 cases the dose had to be increased to 225 mg. daily before abnormal movements were controlled. The first noticeable change was in the emotional upset, followed by an effect on the abnormal movements and finally on muscular coordination, power, and tone: In 3 cases hydroxyzine was replaced by reserpine, 0.6 mg. daily, after Days 8, 14, and 26 respectively, but in no case did this evoke a more rapid response. In the group treated with phenobarbitone no case improved within one week and only one within 2 weeks, while no recovery was recorded within 3 weeks. The main side-effect of treatment in both groups was drowsiness, but ataxia occurred after phenobarbitone treatment, necessitating reduction in dosage in one case.

The authors conclude that hydroxyzine is a valuable drug in the management of chorea, but must be given in daily doses of 150 mg. or more.

B. M. Ansell

CHRONIC RHEUMATISM

1458. Comparison between the Cetavion Test and the Haptoglobin Index in Chronic Rheumatism. (Comparaison du test au cétavion et de l'indice d'haptoglobine dans les rhumatismes chroniques)

J. Badin and J. Martin. Presse médicale [Presse méd.] 70, 76-78, Jan. 13, 1962. 14 refs.

In the test here described from the Centre d'Exploration Fonctionnelle de la Seine, Paris, measurement is made of the turbidity which occurs on adding one volume of the serum being tested to 15 volumes of 1% cetyltrimethylammonium bromide ("cetavlon") adjusted to pH 4·0 with N/10 hydrochloric acid at a temperature of 15 to 16° C.; the reaction mixture is allowed to stand for 2 minutes, then stabilized by the addition of 2·5 volumes of glycerin, shaken vigorously, and read after standing for 30 minutes at room temperature.

The mean value in 94 normal subjects as measured on the Vernes photometer was found to be 10±10 units. In ankylosing spondylitis (22 cases) the mean was 44 units and over two-thirds of the readings exceeded the upper limit of normal (taken as the mean plus 2 standard deviations). Similar values were found in 62 cases of rheumatoid arthritis, both in 25 cases which gave a positive Rose-Waaler reaction and in 37 giving a negative result (means of 53 and 51 units respectively). Sera from patients with degenerative lesions of the intervertebral disks, joints, and ligaments gave normal or nearly normal values, except for 23 cases of osteoarthritis of the hip. in 5 of which (22%) the readings were abnormally high. These results are compared with the haptoglobin index, which gave concordant results. The cetavion test measures the level of serum glycoprotein ["seromucoid" of other authors, and haptoglobin is one of the more important polysaccharide-rich proteins of the serum. The of the increase of total α and β sugar-containing globu-E. G. L. Bywaters ٠.,

1459. Basophil Leucocytes (Blood Mast Rheumatold Arthritis: [In English]

A. A. Boseila and E. C. Toone Jr. Acta rheumatologica Scandinavica [Acta rheum. scand.] 7, 183-190, 1961. 2 figs., 12 refs.

Tissue mast cells are numerous in sites where lesions due to collagen disorders tend to occur. There is evidence of a morphological and-functional relationship between mast cells and circulating basophil leucocytes; the latter may represent the circulating component of the mast-cell system. A study of the changes in the basophil count in a group of 76 patients with rheumatoid. arthritis at various stages and in 46 healthy volunteers is reported from the Medical College of Virginia, Richmond.

Patients with severe rheumatoid arthritis of over 2 years' duration were found, in aggregate, to have a significantly lower basophil count than the controls; in patients receiving steroid therapy the count was even lower: In patients with severe arthritis of less than 2 years' duration the basophil count was slightly, but not significantly, raised, while in those with less severe disease the average count was very little different from that in

It is suggested that the decrease in the number of circulating basophils, which are known to contain acid mucopolysaccharides, is a reflection of a decreased production of these substances in the body in rheumatoid disease. Alternatively, it may be due to increased fragility of the basophils, leading to degeneration; the cells cannot then be identified or counted. B. E. W. Mace

1460. Current Status of the Rheumatold Factor

J. H. VAUGHAN and V. P. BUTLER JR. Annals of Internal Medicine [Ann. intern. Med.] 56, 1-11, Jan., 1962. 6 figs.,

1461. A Fluorescent Test for the Rheumatold Factor In-

E. Hess and M. ZIFF. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 574-578, Dec., 1961 [received Feb., 1962]. 1 fig., 14 refs.

During the course of investigations carried out at the University of Texas Southwestern Medical School, Dallas, (and to be reported elsewhere) on rheumatoid arthritic patients with high titres of rheumatoid factor it was found that leucocytes and platelets in the peripheral blood were coated with the factor. Advantage was taken of this phenomenon to develop a new sensitive test for rheumatoid factor. Fluoresceinated aggregated gamma globulin (Cohn Fraction II) was shown to react with the coating of rheumatoid factor on the leucocytes and platelets. [Full technical details of the technique are given in the paper.] The method does not provide quantitation of the titre.

By means of this procedure positive results were obtained in 81 (90%) of 90 cases of classic and definite adult rheumatoid arthritis, in 13 (81%) of 16 cases of

authors conclude that the cetavion test is a good measure probable and possible rheumatoid arthritis, and in 2 of 3 cases of psoriatic arthropathy. False positive results were observed in a number of hyperglobulinaemic conditions and in 8 of 11 cases of other connective-tissue disorders. In 103 miscellaneous cases, including patients with other arthritic conditions, gout, and rheumatic, fever, and also normal subjects, only one false positive result was obtained. It is stated that this fluorescent technique proved to be more sensitive than the comparative results obtained with the capillary latex fixation test and the sensitized sheep cell test. Harry Coke

1462. Evaluation of Rheumatoid Factor Tests

M. V. WALLER, B. DECKER, E. C. TOONE JR., and R. IRBY. Arthritis and Rheumatism [Arthr. and Rheum.] 4, 579-591, Dec., 1961 [received Feb., 1962]. 32 refs.

The authors report a study of the agglutinating capacity of "rheumatoid factor" by means of three different tests, namely, the Heller modification of the Rose-Waaler sensitized sheep cell (S.S.C.) test, the Hyland F.II latex test, and a sensitized human cell DCe/DCe by a single high titre anti-DC serum (S.H.C. test). Positive results were taken to be indicated by a titre of 1:20 or above in the S.S.C. test, 1:16 or above in the S.H.C. test, and 1:20 or above in the latex test. Sera were obtained at the Medical College of Virginia. Richmond; from 340 blood donors or women attending a prenatal clinic, from 87 patients with rheumatoid arthritis, 43 with other rheumatic diseases, and 30 hospital patients with non-rheumatic diseases.

In rheumatoid arthritis the proportions of positive results were as follows: by the S.H.C. test 82%, the latex test 85%, and the S.S.C. test 68%. The first two methods were more sensitive but less specific. The proportion of false positive results in the three tests were 3.0, 3.0, and 0.3% respectively. The tests were repeated one or more times to exclude transient false positive reactions associated with other intercurrent illnesses. No statistical significance of false positivity in relation to age, sex, or race was found, nor any between the rheumatic and non-rheumatic diseases. Greater positivity in . classic rheumatoid disease was statistically more evident than in the "probable or possible" group, and also in disease in Stages III and IV than in Stages I and II. The mean titre in males was greater than that in females. Positive agglutination in definite rheumatoid arthritis. did not correlate significantly with age, duration of disease, sex, presence of nodules, or race.

-Harry Coke

1463. Clinical Observations on So-called Rheumatoid Carditis. [In English]

A. ROBECCHI and G. EINAUDI. A.I.R. Archives of Interamerican Rheumatology [A.I.R. Arch. interamer. Rheum. (Rio de J.)] 4, 281-293, Sept., 1961 [received Feb., 1962].

The authors examined 420 patients with rheumatoid arthritis who were undergoing treatment at the Turin Rheumatological Centre in an endeavour to establishthe existence, frequency, and type of cardiac abnormality in sufferers from this disease. There were 170 males and 250 females ranging in age between 7 and 78 years. In 59 very severe cases cardiac changes were discovered which the authors consider were attributable to the rheumatoid disease alone—"Theumatoid carditis". They suggest that such lesions can, however, be brought to light only by means of very careful clinical and instrumental examination, as no significant symptoms are generally apparent. They conclude that their findings confirm the systemic nature of rheumatoid arthritis; also that the cardiac lesions which occur in that disease bear no relationship to those which follow rheumatic fever.

W. S. C. Copeman

1464: Observations on a Modified Latex Fixation Test H. SEIFERT. A.I.R. Archives of Interamerican Rheumatology [A.I.R. Arch. interamer. Rheum. [Rio de J.)] 4, 294-310, Sept., 1961 [received Feb., 1962]. 6 refs.

The author has shown by absorption tests that the latex-fixation test as modified by him is closely related to the L-agglutination test, thus indicating that a streptococcus-agglutinating factor is present in rheumatoid arthritis. He concludes that the Rose-Waaler and gamma-globulin reactions demonstrate the presence of the agglutination-activity factor and the Lagglutination factor, and the latex test the presence of a streptococcus-agglutinating factor. The latex test does not, however, prove the presence of agglutination-activating factor. He points out the importance of determining whether the streptococcus-agglutinating factor is the cause or the consequence of rheumatoid arthritis.

W. S. C. Copeman

1465. The Latex Fixation Test in Rheumatic Diseases: a Review...

J. M. Singer. American Journal of Medicine [Amer. J. Med.] 31, 766-779, Nov., 1961. Bibliography.

1466. Investigations into the Specificity of Four Antigenic Serum Factors Isolated in Primary Chronic Rheumatism with Special Reference to Their Immune Activity. (Spezifitätsunitersuchungen an 4 bei primär chronischem Rheumatismūs isolierten antigenen Serumfaktoren mit besonderer Berücksichtigung ihrer Immunleistungen) H. Seifert. Zeitschrift für die gesamte innere Medizin und ihre Grenzgebiete [Z. ges. inn. Med.] 16, 1066–1073, Dec. 15, 1961. 7 refs.

This is a further report by the author from the Institute for Rheumatology, Dresden, on the differentiation and characterization of antigenic serum factors in rheumatoid arthritis. In previous papers the differentiation of a rheumatoid arthritis factor from a streptococcal agglutinating factor was reported; in the present investigation four antigenic factors were isolated and a specific antiserum prepared in rabbits against each antigen which precipitated the antigen without affecting any of the other antigens. Usually 2 of the antigenic factors were found together in the same serum. The main features of the antigens were as follows. (1) A cold-precipitated haemagglutinating antigen; this factor gave a positive Rose-Waaler reaction and y-globulin test. (2) A coldprecipitated antigen giving a positive latex fixation reaction. (3) An antigen precipitated at room temperature

which agglutinated streptococci. (4) An antigen precipitated at room temperature which gave a positive latex fixation reaction.

The technique used for separating the four factors is described in detail. The exact relationship of these antigens to rheumatoid arthritis is not yet determined, but investigations in progress show that still further antigens are present in the serum of patients with the disease. The highly specific nature of the four antigens as tested by antigen—antibody reactions is stressed.

G. W. Csonka

1467. Relation of Toxic Reactions in Gold Therapy to Improvement in Rheumatoid Arthritis: a Report

THE RESEARCH SUB-COMMITTEE OF THE EMPIRE RHEUMA-TISM COUNCIL. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 335–340, Dec., 1961. 2 refs.

An investigation was carried out to determine whether patients with rheumatoid arthritis in whom toxic reactions developed during gold therapy obtained remission of the arthritis more frequently in consequence. All the 159 patients studied had had gold therapy for 5 months and been followed up for 30 months [see Abstract 1468], 77 (31 toxic and 46 non-toxic) having received a total dose of 1 g. of sodium aurothiomalate and 82 controls ("12 toxic and 70 non-toxic") a total dose of 0.01 mg. At the start of treatment both groups were comparable in all main essentials.

On the basis of the criteria used (functional capacity estimated by the doctor, the patient's own estimate of fitness, effect on joint lesions, and strength of grip) no evidence was obtained that patients experiencing toxic reactions fared better than those who did not. In fact, the number of joints affected as assessed at 12 months was higher in the toxic patients than in the non-toxic at a time when the maximum benefit from gold therapy was to be expected.

It is concluded that there is no evidence for the commonly held belief that toxic reactions during gold therapy increase the probability of a remission. D. Preiskel.

1468. Gold Therapy in Rheumatold Arthritis. Final Report of a Multicentre Controlled Trial

THE RESEARCH SUB-COMMITTEE OF THE EMPIRE RHEUMATISM COUNCIL. Annals of the Rheumatic Diseases [Ann. rheum. Dis.] 20, 315–334, Dec., 1961. 2 refs.

The study herein reported is a continuation of the investigation carried out by the Empire Rheumatism Council in 1960 in which it was shown that patients with active rheumatoid arthritis treated over a period of 5 months with a total dose of 1 g. of sodium aurothiomalate fared better, except radiologically, than patients who received only 0.01 mg. during the same period. The patients have now been followed up for another year—that is, 2 full years after the last injection and 2½ years after the trial began. The final analysis is based on the follow-up findings in 159 patients, aged 20 to 64 years, 77 of whom received the higher dose of gold and 82 (controls) received the smaller dose. In 16 of the former group and in 20 controls a second course of injections was started at month 18 (from the start of the

trial), but subsequently 2 of the controls were excluded from the trial.

During the first course of injections side-effects developed in 35 of the gold-treated patients and in 16 controls. Of the 16 gold-treated patients receiving a second course. 3 experienced side-effects, while only one of the 20 controls was similarly affected, the commonest complication being dermatitis. Functional capacity was assessed by the physician on 5 grades and the patient's own estimation of his fitness was expressed as a percentage. After 30 months the former's estimate of the efficacy of gold tended to be slightly more optimistic than that of the patient. Although at 18 months the gold-treated patients appeared to fare better as regards joint lesions, at 30 months this advantage had been lost. Similarly, measurement of strength of grip (in mm. Hg) and estimation of the haemoglobin level, erythrocyte sedimentation rate, and leucocyte count showed no significant difference between treated cases and controls.

It is stated that since the main reason for giving a second course of gold was failure to respond to the first, it may be assumed that these patients formed relatively "bad" groups, and treated patients therefore fared no better than controls.

D. Preiskèl

COLLAGEN DISEASES

1469. Renal Damage in the Course of Visceral Lupus Erythematosus (Lupus Nephritis). (Zmiany nerkowe w toczniu rumieniowatym układowym (Lupus Nephritis))
S. HOROSZEK, L. MIRECKI, and J. STOLARCZYK. Polski Tygodnik Lekarski [Pol. Tyg. lek.] 16, 1853–1857, Nov. 27, 1961 [received Feb., 1962]. 4 figs., 12 refs.

It has been reported in the literature that between 69 and 100% of all patients suffering from disseminated lupus erythematosus develop renal complications (lupus nephritis) in the course of their illness. The authors, on the basis of observations made by Muchreke et al: (Lupus Nephritis, Baltimore, 1957), classify these patients in the 4 following clinical groups. (1) Mild nephritis, in which albuminuria and microscopical haematuria occur, but renal function remains unimpaired and the prognosis is good. (2) Severe nephritis; here in addition to albumin and blood in the urine, casts are also present, and renal function may be severely affected, progressing to uraemia and death in a large proportion of patients. (3) The nephrotic syndrome, the existence of which entity is disputed by many authors; in this type the renal symptoms overshadow the clinical picture, the diagnosis often being made on histological examination of a renal biopsy specimen, while the plasma globulin and blood urea levels are frequently raised. (4) Pseudonephrotic syndrome, in which there is typically a low blood cholesterol level; the outcome in this type of renal involvement is commonly fatal within weeks or months of the onset of the disease:

The authors describe 2 personal cases. In one the patient had mild nephritis and is still alive after 3 years; the other, however, was suffering from the pseudo-

nephrotic syndrome and died 16 weeks after onset of the illness. Post-mortem findings and photomicrographs of the renal lesions are presented in detail. The value of steroid therapy of lupus nephritis is discussed.

A. I. Suchett-Kaye

1470. Value and Significance of Antinuclear Antibodies for the Diagnosis of Lupus Erythematosus and the General Conception of the Disease. (Valeur et signification des anticorps anti-nucléaires pour le diagnostic du lupus érythémateux et la conception générale de la maladie lupique)

M. SELIGMANN. Semaine des hôpitaux de Paris, [Sem. Hôp. Paris] 38, 60-63, Jan. 2, 1962. 2 refs.

In this paper—one of 15 forming a symposium devoted to systemic lupus erythematosus—the author, working at the Hôpital Saint-Louis, Paris, reviews work on antinuclear antibodies. Antibodies against deoxyribose nucleic acid were found in 28 out of 32 sera of untreated patients with systemic lupus erythematosus, 26 out of 79 sera of patients who had been treated but were not in remission, but in none of the 23 sera of patients in remission. No positive results were obtained in ratients with chronic discold lupus, rheumatoid arthritis, and diseases characterized by a raised serum y-globul:n content.

G. L. Asherson

1471. Disseminated Lupus Erythematosus in Childhood. (Le lupus érythémateux disséminé de l'enfant)
P. ROYER. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 38, 40-45, Jan. 2, 1962. 2 figs., 10 refs.

At the Hôpital des Enfants-Malades, Paris, the author has studied 12 children, of whom 9 were girls, suffering from systemic lupus erythematosus. He confirms that the disease affects predominantly females in childhood as well as in adult life. The clinical picture resembles that seen in adults.

G. L. Asherson

1472. Disturbances of Metabolism of the Aromatic Amino-acids in Collagen Disease. Their Relation to the Conception of Lupoid Disease. (Troubles du métabolisme des acides aminés aromatiques dans les collagénoses. Leur apport dans la conception de la maladie lurique) C. GRUPPER, J. C. LEGRAND, and P. GONNARD. Semaine des hôpitaux de Paris [Sem. Hôp. Paris] 38, 70-76. Jan. 2, 1962. 21 refs.

In this third study [see Abstracts 1470 and 1471] carried out at the Hôpital Saint-Louis, Paris, the authors confirmed the Japanese finding that patients with systemic lupus erythematosus, chronic discoid lupus, dermatomyositis, scleroderma, morphoea, and rheumatoid arthritis excrete 2:5-dihydroxyphenylpyruvic acid. This acid is not found in the urine of normal subjects and its abnormal excretion is apparently not due to the administration of salicylates. The authors suggest that the colagen diseases can be regarded as metabolic diseases due to enzyme abnormality. Some degree of improvement was observed in a few patients with acute systemic lupus erythematosus when they were given a diet with a low phenylalanine content.

G. L. Asherson

Physical Medicine

1473. Rigidity and Spasticity in Man: Electromyographic Analysis with Reference to the Role of the Globus Pallidus

H. SHIMAZU, T. HONGO, K. KUBOTA, and H. NARA-BAYASHI. Archives of Neurology [Arch. Neurol. (Chic.)] 6, 10-17, Jan., 1962. 8 figs., 15 refs.

The physiological basis of the effect of pallidotomy on Parkinsonian rigidity and the rigidospastic states of cerebral palsy is analyzed by electromyographic recordings of the patterns of stretch reflex and the study of intervals between each NMU [neuromuscular unit] discharge, as originally proposed by Tokizane, before and after pallidotomy.

For rigidity and similar muscular states associated with a tonic pattern of the stretch reflexes, pallidotomy is effective, presumably due to reduction of a hyperactive gamma system. Spasticity, which is characterized by a phasic pattern of the stretch reflexes, is not significantly influenced by pallidotomy, but may be modified by some other lesions.—[Authors' summary.]

1474. Effect of Percutaneous Medication on Muscle Tissue: an Electromyographic Study

B. S. Post. Archives of Physical Medicine and Rehabilitation [Arch. phys. Med.] 42, 791-798, Dec., 1961 [received Feb., 1962]. 4 figs., 16 refs.

The author describes an electromyographic technique designed to determine whether percutaneous absorption is in fact effective in depositing a drug in the deeper tissues. The method was tested at the Downstate Medical Center, Brooklyn, New York, by observing the effects of a rubefacient applied to the skin upon the rate of muscle fatigue. The experiment was carefully planned so as to lessen the influence of the many variables, such as the differences in the size, strength, and development of the muscles in different persons on the results. The muscle function tested was the isometric contraction of the triceps, which was measured electromyographically using surface electrodes 1 cm. in diameter, the active electrode being positioned half way along a line from the posterior axillary fold to the lateral humeral epicondyle and the reference electrode 5 cm. distally along the same

In all, 285 male subjects were examined by the following procedure. The subject was seated before an apparatus designed so that extension of the triceps lifted a heavy weight over so short a distance that a virtually isometric contraction resulted, the weight chosen for each person being such as to fatigue the muscle in approximately 2 minutes. As the muscle contacted isometrically for 2 minutes the amplitude and shape of the tracing were observed and recorded on magnetic tape. After the 2-minute contraction the subject rested for one minute, following which he again performed the isometric contraction until fatigue set in, the entire process being repeated for 34 minutes. It was found that the fatigue

point usually reached a plateau after about 10 minutes of testing.

Some of the subjects were then retested as follows; when the fatigue plateau had been reached and maintained for "ten fatigue periods" the triceps muscle was sprayed with a rubefacient and the test continued. Others were re-examined 15 minutes after the rubefacient had been sprayed on. Control tests using a water spray instead of the rubefacient were also performed. These tests showed that the rubefacient spray definitely increased the time taken to fatigue the working muscle and that the water spray had no such effect. The muscle also appeared to increase its capacity for work shortly after the rubefacient spray was applied. The author claims that these results indicate that percutaneous absorption of a drug does occur. Kenneth Tyler

1475. The Training and Movement Treatment of the Arthritic Deformed Hand. [In English]

G. EDSTRÖM. Acta rheumatologica Scandinavica [Acta rheum. scand.] 7, 249-260, 1961 [received Feb., 1962]. 11 figs., 1 ref.

In Sweden 20 years ago flexion contracture of the knee was the most common deformity encountered in rheumatoid arthritis, but now a relatively common disability is deformity of the hands with poor grip and inability to oppose the thumb and fingers. To minimize such disabilities the author of this paper from University Hospital, Lund, recommends the encouragement of active movements and heat therapy. As the activity of the disease varies from time to time, the balance between rest and movement should be controlled accordingly. Flexibility of the fingers must be preserved, and for this purpose self-help devices such as hand strengtheners are of special value. Pieces of rubber, rhythmically compressed between the fingers, can be employed for exercising the small muscles. Switching on a circuit-breaker and turning keys or taps are useful exercises, not only for the finger muscles, but also for the wrist. If the proximal interphalangeal joints are fixed in hyperextension a training apparatus is required for maintaining the plus position.

Nodular thickening of the flexor tendons of the fingers may cause locking, and when this occurs relief may be obtained by injecting cortisone into the tendon sheaths, though surgery may also be required. Wrist movements can be improved by rolling and unrolling a cord attached to a rod, strength of movement being modified by attaching various weights to the cord. Arthrodesis is sometimes performed in order to restore function, especially in cases of destruction of the metacarpophalangeal joint of the thumb. When bone and joint destruction is extensive the wrist should be fixed in dorsal flexion with the aid of splints, plaster, or bandage. Surgery is indicated in the management of fixed volar flexion.

A. Garland

Neurology and Neurosurgery

1476. An Investigation of Some Therapeutic and Physiological Effects of Perphenazine in Huntington's Chorea. [In English]

H. Merskey, T. Rice, and A. Troupe. Psychophar-macologia [Psychopharmacologia (Berl.)] 2, 436-445, 1961. 1 fig., 15 refs.

Many drugs have been used to limit the range and frequency of the involuntary movements in patients with Huntington's chorea and this paper from Cherry Knowle Hospital, Ryhope, Sunderland, reports the effects of perphenazine in 4 patients (one woman and 3 men aged 46 to 56) with this disease. The dosage ranged from 8 to 24 mg. 3 times a day for 3 to 4 weeks and throughout this time clinical observations, cinematography, and various tests of manual dexterity were carried out. The 4 cases are briefly described. Cinematography showed that the drug did reduce the range and frequency of the involuntary movements and improved the gait and motor abilities of these patients, though only in one case was this improvement apparent clinically. In addition, the speed in performing a motor task was reduced, suggesting that the improvement in the chorea might be due to the development of muscular rigidity of a Parkinsonian type. This possibility is discussed. B. M. Davies

1477. Frontal Epileptogenic Foci and Their Clinical Correlations

L. Fegersten and A. Roger. Electroencephalography and Clinical Neurophysiology [Electroenceph. clin. Neurophysiol.] 13, 905-913, Dec., 1961 [received Feb., 1962]. 4 figs., 9 refs.

Of the electroencephalograms (EEGs) recorded from some 10,000 patients at the Hôpital la Timone, Marseilles, over the past 4 years only 30 satisfied the authors' criteria for frontal epileptogenic foci. These criteria were purely electroencephalographic, namely, discharges of spikes localized in the fronto-polar region only, or simultaneously recorded from the fronto-polar region and the superior frontal, median-frontal, or inferior-frontal regions. Of the 30 patients, 17 presented a right frontal epileptic focus and 13 a left frontal focus. In 10 cases the spike discharges were limited to the fronto-polar region, in another 10 simultaneous spikes were recorded from the fronto-polar, superior-frontal, and medianfrontal regions, while in the remaining 10 the discharges were simultaneously visible in the fronto-polar and superior-frontal regions as well as in the inferior-frontal region. In all but one of the cases underlying slow activity was recorded from the frontal region in question, and in only 9 instances was the background activity normal over the rest of the scalp. Noting with interest and surprise that EEG seizure discharges were recorded in as many as 10 out of the 30 patients, such discharges occurring spontaneously during recording in 5 of them, the authors point out the relative rarity of spontaneous seizure discharges in the temporal region compared with the frequent recording of temporal epileptogenic activity. They suggest the possibility that the ratio of infra-clinical to clinical seizures is higher in patients with frontal-lobe lesions producing epilepsy than in patients with temporal-lobe epilepsy.

The types of seizures experienced by the patients are described and discussed. It was found, in agreement with previous workers, that the largest group (14 out of the 30) was made up of those with adversive seizures. Somatomotor seizures (10 cases) were the most common among the others, while 6 of the patients had experienced no epileptic phenomena at all. Of known aetiological factors, open frontal head injury was much the most frequent (16 cases), followed by cerebral tumour (5), encephalitis (3), and cerebral haemorrhage (2). Of the 16 patients suffering from open head injury, 9 had been operated for this, and these all became epileptic, with a latent period varying from a few days up to 8 years. In no case was there evidence of birth injury or closed head injury later in life and it is emphasized that closed head injuries rarely result in frontal epileptogenic activity.

Peter Leyburn

1478. Precipitating Factors in the Pathogenesis of Amyotrophic Lateral Sclerosis. [In English]

E. ASK-UPMARK. Acta medica Scandinavica [Acta med. scand.] 170, 717-723, Dec., 1961. 38 refs.

The pathogenesis of amyotrophic lateral sclerosis was studied in 91 cases observed in 10 hospitals in Sweden; between 1927 and 1960. The author estimates that the annual incidence of the disease is one in 100,000 individuals and that one death in 1,000 in Sweden is due to amyotrophic lateral sclerosis.

As regards precipitating factors, no correlation was found with diabetes or exogenous allergy. However, three factors are suggested as being of importance: undue strain on the neuromuscular units, malnutrition (the term being used in its widest sense), and, possibly, spinal anaesthesia.

G. S. Crockett

1479: Deglutition in Myasthenia Gravis J. P. Murray. British Journal of Radiology [Brit. J. Radiol.] 35, 43-52, Jan., 1962. 4 figs., 10 refs.

Deglutition in myasthenia gravis was studied radiologically in 23 patients at the David Lewis Northern and Sefton General Hospitals, Liverpool, conventional fluoroscopy being used in 13 patients and cinefluorography in 10. There were no complications from the examination, although additional care was necessary when there was notable bulbar involvement. The author states that demonstrable abnormalities of deglutition are almost invariably present and can be clearly and permanently recorded by cinefluorography. Reference is made to the value of drugs in diagnosis; in this

series the effects of "tensilon" were transient, neostigmine and mestinon (pyridostigmine) being considered more useful. [The reproductions of the cinephotographs are poor.] Hugh Garland

1480. Observations on the Cardiovascular Involvement, Including the Cardiac Conduction System, in Progressive Muscular Dystronhy

T. N. JAMES. American Heart Journal. [Amer. Heart J.] 63, 48-56, Jan., 1962. '8 figs., 29 refs...

There are many reports in the literature of involvement of the heart in muscular dystrophy; this involvement is important clinically since cardiac arrhythmia and sudden death are common in this disease. The author, from the Henry Ford Hospital, Detroit, describes the findings in a 19-year-old male suffering from pseudohypertrophic muscular dystrophy, who died suddenly with acute dyspnoea, cardiac arrhythmia, and heart block. At necropsy there were degeneration of the fibres of the sinus node and an unusual non-inflammatory degeneration of the arteries which supply both the sinus and the atrioventricular nodes and of some other arteries. The pathogenesis of the arrhythmia and heart block is discussed. R. Wyburn-Mason

BRAIN AND MENINGES

1481: Behaviour after Cerebral Lesions in Children and

H. L., TEUBER and R. G. RUDEL. (Developmental Medicine and Child Neurology [Develop. Med. Child Neurol.] 4, 3-20, Feb., 1962. 11 figs., 28 refs.

Animal experiments tend to show that brain injuries sustained early in life have less effect than comparable lesions incurred at later stages. By contrast, neurological observations suggest that certain forms of early brain damage in children may have disproportionately serious consequences for later development. The apparent contradiction may be resolved if one grants that results might differ, according to (a) the kind of task employed, and (b) the age at which the child is tested. Three perceptual tasks have been devised which disclose such differential effects.

On one task, the effects of early injury are not apparent before the age of 11 years, but become increasingly obvious thereafter. On the second, a deficit is manifest at all ages. The third reveals effects of early injury only up to the age of 11 years; no abnormality can be discovered after this age.—[Authors' summary.]

1482. Prophylaxis of Frequent Vascular Headache with Methysergide

A. R. HALE and A. F. REED. American Journal of the Medical Sciences [Amer. J. Med. Sci.] 243, 92-98, Jan., 1962. '1 fig., 8 refs.

An attempt has been made at the Charity Hospital of Louisiana, New Orleans, to reduce the frequency of "vascular headache" by the use of the anti-serotonin agent methysergide (UML-491). Taking part in the trial were 57 patients with frequent attacks of migraine

as well as 8 with "cluster headache". Of the migrainous patients without associated neuroticism, 69% responded favourably with either complete remission or total reduction in severity and frequency of attacks. About onethird of the patients had mild and transient side-effects, the women being especially prone. In some patients electroencephalographic abnormalities were said to be reversed. Only one case is reported in detail; this patient received 6 mg. of UML-491, at first and subsequently 2 mg. daily over a period of 19 months.

[The term "cluster headache" will not be understood by many readers in Great Britain. It is perhaps unfortunate that the word "seizure", which was once used as a synonym for "stroke" and more recently to denote an epileptic attack, is in this paper used to describe an episode of headache. In view of the frequency and erratic course of migraine the number of patients observed is perhaps hardly significant.]

Hugh Garland

1483. Studies on Headache: the Relevance of the Prophylactic Action of UML-491 in Vascular Headache of the Migraine Type to the Pathophysiology of This Syn-

D. J. DALESSIO, W. A. CAMP, H. GOODELL, L. F. CHAP-MAN, T. ZILELI, A. O. RAMOS, R. EHRLICH, F. FORTUIN, McK. CATTELL, and H. G. Wolff. World Neurology [Wld Neurol.] 3, 66-71, Jan., 1962. 7 refs. /

Administration of UML-491 (1-methyl-p-lysergic acid butanolamide bimaleate) may reduce the number and severity of migrainous attacks, although it does not help the actual attack. This phenomenon has been investigated at the New York Hospital-Cornell Medical Center, New York, in the hope of elucidating the mechanism of migraine.

While UML-491 is known to have anti-serotonin action, the evidence that serotonin is involved in migraine is not conclusive. Although in occasional patients UML-491 causes severe peripheral vascular insufficiency, it is unlikely that its prophylactic action is by inducing a persisting vasoconstrictor state. It does, however, potentiate other vasoconstrictors. It has a definite antiinflammatory action; it also has the effect of generally reducing cerebral activity and mildly damping down vasoconstrictive reflexes.

The authors conclude that the significant action of. UML-491 is in reducing the magnitude of cranial vascular responses, and that this finding gives further support to the theory that unstable cranial vasomotor function is a prime factor in migraine. N. S. Alcock

1484. Medical Treatment of Spontaneous Intracranial Hemorrhage by the Use of Hypotensive Drugs · ; -7. J. S. MEYER and R. B. BAUER. Neurology [Neurology (Minneap.)] 12, 36-47, Jan., 1962. 40 refs.

Between January 1, 1958, and June 30, 1960, a total of 312 patients in whom subarachnoid haemorrhage was diagnosed were admitted to Detroit Receiving Hospital. -In 79 a ruptured aneurysm was the cause of the haemorrhage, in 167 there was hypertensive intracerebral haemorrhage, and in 11 there were other causes for the

haemorrhage; in 55 cases the aetiology was not known. In an attempt to assess the value of hypotensive therapy in recent intracranial haemorrhage some two-thirds of the patients, including all those who were admitted to the neurology service of the hospital, received reservine, first by injection and subsequently by mouth, with the object of maintaining the blood pressure at a normal \ level. The remaining one-third, all of whom were admitted to the general medical wards, acted as a control group; they did not receive reserpine but in all other respects were treated in the same way. The groups were comparable as regards age, actiology of the haemorrhage, and severity of the clinical picture. Hypotensive therapy was thought to have been adequate in only 84 of the patients to whom it was administered, and in 128 it was considered inadequate for various reasons. The mortality in hospital among the patients with ruptured aneurysm was 61.5% in those adequately treated, 70% in those inadequately treated, and 90% in the untreated group. These differences are described as indicating a - promising trend but they are not statistically significant. Among the patients with primary intracerebral haemorrhage the mortality was 63% in those adequately treated, 85% in those inadequately treated, and 98% in the untreated group. These differences are highly significant. Of the patients with haemorrhage of unknown cause 84% of those adequately treated, 75% of those inadequately treated, and 100% of the untreated group died. The authors conclude that hypotensive medical treatment is advisable in the acute phase of spontaneous intracranial haemorrhage, particularly if the blood pressure is raised. Bernard Isaacs

1485. Involuntary Movements in Patients with Intracranial Tumors: Their Occurrence and Possible Pathogenesis

J. CHOROBSKI. Archives of Neurology [Arch. Neurol, (Chic.)] 6, 27-42, Jan., 1962. 9 figs., bibliography.

It is pointed out that although extrapyramidal syndromes are most frequently seen in association with infection, intoxication, vascular lesions, or disturbances of brain metabolism, they also occur with tumours, when they are usually less bizarre than in other conditions. In many patients they disappear promptly when the tumour is removed. Analysis of the literature shows that while cases have been reported in which these movements and alterations of tone have been associated with tumours of the basal ganglia, there are others in which one or both have been destroyed without producing such symptoms or in which the tumours were elsewhere than in or near the basal ganglia.

In this paper from the Academy of Medicine, Warsaw, the author describes 14 cases (3 of them in detail) in which involuntary movements were due to intracranial fumours. In 11 of the patients the movements stopped when the tumour was removed—immediately after operation in 8 and within 1 to 6 weeks in 3. There did not appear to be any correlation between the site of the tumour and the movements. One child had bilateral tremor with total invasion of one basal ganglia but no abnormality on the other side.

As regards the mechanism of these involuntary movements the author considers it likely that they "may result when there is a disturbance in the innervation necessary for the maintenance of any body posture and of any motor act". The afferent side does not seem of primary importance. This disturbance may be in the everebreating circuits which may interfere with the smooth cooperation of the pyramidal and extrapyramidal systems:

N. S. Alcock

1486. Self-induced Epilepsy: a Collection of Self-induced Epilepsy Cases Compared with Some Other Photoconvulsive Cases

K. Andermann, S. Berman, P. M. Cooke, J. Dickson, H. Gastaut, A. Kennedy, J. Margerison, D. A. Pond, J. P. M. Tizard, and E. G. Walsh. *Archives of Neurology [Arch. Neurol. (Chic.)]* 6, 49-65, Jan., 1962. 3 figs., 30 refs.

Twenty cases of self-induced epilepsy are presented and compared with similar cases from the literature and a group of 13 light-sensitive epileptics. [These cases were collected from Britain, France, South Africa, and the U.S.A.]

Self-induced epilepsy is, in fact, very rare. The selfinducing group appears to have an exceptionally high. light sensitivity and frequent seizures, and its members often are of substandard intelligence. The majority of self-inducing epileptics exhibit seizures of the petit mal. or petit mal and myoclonic variety. The degree of impairment of consciousness is variable. The seizures are frequent, but depend to a certain extent on the light intensity available. Spatial displacement may be as important a cause for eliciting seizures as temporal lightdark sequences. A variety of causes may suffice for the act of self-induction; there is no single necessary cause. The majority of patients show some form of multiple spike-and-wave activity. A shortened spike interval and spike duration may be the cause for the excessive sensitivity to light changes and a condition for self-incuction to occur.—[Authors' summary.]

1487. Cerebellar Degeneration with Clinical Manifestation in Chronic Epileptic Patients. [In English]

C. HABERLAND. Psychiatria et neurologia [Psychiat. et Neurol. (Basel)] 143, 29-44, 1962. 9 figs., 31 refs.

Clinical and pathological reports are presented from the Illinois State Psychiatric Institute, Chicago, of 3 patients with epilepsy who developed a progressive cerebellar syndrome before death. Histo-pathclogical studies showed a diffuse degeneration of the cerebellar cortex in each case and the author discusses the possible actiology of the lesion. In none of the cases was there evidence of a familial incidence of cerebellar disease and in an attempt to link the epilepsy with cerebellar lesions the author considers two possibilities: (1) the cerebellar lesions might be the result of anoxia accompanying frequent epileptic seizures; or (2) the prolonged administration of "dilantin" (phenytoin sodium) as an anticonvulsant in these cases might have produced histological changes in the cerebellum, as it has been shown experimentally to do in cats. J. B. Stanton

Psychiatry

1488. Severe Psychiatric Disturbances in the Postoperative Period—a Five-year Survey of Belfast Hospitals S. J. KNOX. *Journal of Mental Science [J. ment. Sci.]* 107, 1078–1096, Nov., 1961 [received Jan., 1962]. 1 fig., bibliography.

Writing from the Queen's University, Belfast, the author first presents an extensive review of the literature of severe psychiatric disturbance in the postoperative period, and then discusses its relevance to the disorder as seen in patients subjected to operation in the Belfast hospitals over a 5-year period, with particular reference to cataract extraction and gynaecological and cardiac surgery. The incidence reported in the literature has varied from 1 in 250 to 1 in 1,500 patients. Disturbance following cataract extraction may be related to the necessary blindfolding after the operation, to sensory isolation, or to an incipient dementing process. Other possible causes include additional drugs and social factors. He next discusses the psychological implications of hysterectomy and the postulated common symptomatology in postoperative psychoses of agitation and depression. Serious psychiatric disturbance has often been observed to follow mitral valvotomy. An anaesthetic may be incriminated in some cases, especially nitrous oxide. Old age, alcoholic excess, and psychogenic factors may also operate as causal factors.

The clinical records of the two psychiatric units in Belfast were examined for the 5-year period January, 1956, to December, 1960. Following a total of 57.600 major operations the incidence of psychiatric disturbance severe enough to require admission to a special unit was 36 cases, an incidence of 1 in 1,600 operations. Of these 36 patients (21 female and 15 male) the greatest. proportion (7 cases) were aged 41 to 45 years. Mitral valvotomy was found to be highly represented (7 cases). No uniform clinical presentation was recognized. The diagnoses conformed to the following categories: depression (13 cases), confusion (12), schizophrenia (9), and mania (2 cases). In no case could the anaesthetic be regarded as the primary cause. Neither duration of stay in hospital before operation nor previous operations made any apparent difference. Constitutional predisposition suggested itself from an increased incidence of significant family history in some of these patients.

J. S. Bearcroft

1489. Psychological Tension in Pregnancy
E. R. Grimm. Psychosomatic Medicine [Psychosom. Med.] 23, 520-527, Nov.-Dec., 1961. 14 refs.

This investigation reported from New York Hospital—Cornell Medical Center, New York City, was designed to discover whether psychological tension in pregnant women varied at different stages of pregnancy and whether it could be correlated with any other measurable factor in the pregnancy, the delivery, or the child.

In the first part of the study five groups of pregnant women, each group of 40 being at different stages of pregnancy, were subjected to psychological testing, the groups being matched according to eight criteria. The subjects were given 5'Thematic Apperception Test cards and were also asked to draw "a person". An index of tension occurred in women in the latter half of the last trimester. The second part of the study entailed the analysis of the test records of 227 pregnant women.

A significant positive correlation was observed between high tension scores and excessive gain in weight during pregnancy as well as a lengthy stage of labour in multiparae. Of the children born to a group of 11 women with extreme tension a significantly high number died or were deformed. The author suggests that the technique employed in this investigation promises a means of identifying women who are likely to experience obstetrical difficulties in which emotional factors play a part.

, A. Balfour Sclare

1490. The Relation between Brain Injury in Early Infancy and Neurosis in Childhood and Adolescence. (Die Beziehungen zwischen frühkindlicher Hirnschädigung und Neurosen im Kindes- und Jugendalter)

W. T. WINKLER. Zeitschrift für Psychotherapie und medizinische Psychologie [Z. Psychother. med. Psychol.] 12, 1-10, Jan., 1962. 11 refs.

At the Children's Department of the University Psychiatric Clinic, Tübingen, the application of Kretschmer's theories has encouraged a multidimensional evaluation of diseases, special attention being paid to psychogenic and external causes as much as to an endogenous, and especially constitutional, actiology. The author of this paper presents his impression of the contribution which minor brain damage of early origin makes to the clinical picture in neurotic children and adolescents. (An accurate statistical report on this problem is promised later when accumulated data have been fully analysed.) In eliciting a patient's history, special inquiry is made regarding such matters as the mother's health during the second half of pregnancy, the duration and complications, if any, of the labour and patient's birth, and his neonatal behaviour.

It was shown that infections of the mother, affecting the child's brain in the second half of pregnancy, birth trauma, and asphyxia were the most frequent findings. Malnutrition and infections involving the brain in the first postnatal year were less often encountered. The damage suffered by the brain may be so inconspicuous that only consideration of all available data, including the results of air studies and electroencephalography, may reveal it. Certain anomalies of physique may result from such encephalopathies. For instance, the "digital bayonet sign" may be present; this becomes apparent when, on the patient spreading his fingers, over-extension at the middle joint of a finger and extension in the ter-

minal joint are seen. Skull dysplasias, such as a hydrocephalic shape, various asymmetries, or hypoplasia of the middle facial region, are sometimes found.

-Psychopathologically, the patient often displays increased irritability, lability of mood, enhanced fatiguability, and heightened reactivity of the vegetative system. In some cases there is a general retardation of intellectual development, while in others there may be aspecific reading or calculating disability or a discrepancy between the scores for verbal and performance tests of intelligence. These children are often distractable, impulsive, inconsiderate, and asocial. Occasionally there is a lack of spontaneity, movements may be clumsy and badly coordinated, and facial mobility-is often reduced. > It is noted, however, that not all the symptoms shown by these patients can be attributed to the encephalopathy of early origin. The handicaps from which the children suffer may arouse punitive tendencies in their parents which, in turn, provoke psychogenic reactions in the patients (enuresis, nightmares, or stealing). An explanation of the organic origin of the children's difficulties may alter the parents' attitude and thus improve the clinical picture in the child. F. K. Taylor,

1491. Treatment of Mentally Retarded with Haloperiodole: with Special Reference to the Counteraction of the Extrapyramidal Symptoms Occurring in Connection with this Treatment. [In English]

E. KIVALO and G. AMNELL. Annales paediatriae Fenniae [Ann. Paediat. Fenn.] 7, 320-328, 1961. 7 refs.

Haloperidol (haloperiodole) was tried on 40 patients at the Institute for the Mentally Retarded, Rinnekoti, Helsinki, the symptoms for which treatment was given including motor unrest, violence, grave insomnia with restlessness, self-injury, and tearing of clothes. All the patients had been treated previously with such neuroleptic drugs as chlorpromazine, thioridazine, reserpine, promazine, and ataractica of several types with only transitory benefit or partial improvement. Of the 40 patients 37 were idiots and 3 imbeciles. An initial dose. of 0.3 mg. of haloperidol 3 times a day was cautiously increased at one-week intervals until an adequate therapeutic dosage was reached; the highest dosage was 1.2 mg. 3 times a day but the average was 0.8 mg. The duration of treatment varied from 1 to 7 months (mean 4-4 months).

The results were good in 33 patients and satisfactory in 5; the good effects related to motor unrest (22 patients), aggression (14), insomnia (10), self-injury (6), destruction of clothes (3), and vomiting (1). In 9 cases symptoms recurred and the dosage in 8 of them had to be increased after 1 to 5 months. Good results were obtained in 7 with the higher dosage; in the eighth case treatment was stopped for two months, but when it was resumed the results were again good.

Side-effects were observed in 23 cases, including bradykinesia in 12, tremor in 5, sialorrhoea in one, oculogyric crises in 6, clonic muscle spasms in 8, trismus in one, and anxiety in 2. The mean dosage (0-05 mg. per 'kg. body weight) was the same in the group with side-effects as in those without. Jaundice occurred in one

case but disappeared on withdrawal of the drug. Orphenadrine hydrochloride in a dosage of 50 mg. 3 times daily was given to 16 patients with Parkinsonian symptoms; the results were good in 11 and satisfactory in 3. A beneficial effect was noted in 3 out of 5 patients given caramiphen (6.25 mg. 3 times a day).

The authors conclude that haloperidol is a "nighly efficient drug" for gravely restless oligophrenic patients.

G. de M. Rudolf

1492. Denial of Alcoholism as an Obstacle to Recovery R. A. Moore and T. C. Murphy. Quarterly Journal of Studies on Alcohol [Quart. J. Stud. Alcohol] 22, 597-609, Dec., 1961. 28 refs.

Denial of his illness is characteristic of the alcoholic. denial, for the purpose of this paper, being defined as "an unconscious attempt to treat external reality as if it did not exist". The authors, finding difficulties in treating cases of alcoholism in which denial was a prominent feature and stimulated by frequent references in the literature to the problem but no attempt at confirmation, undertook the present study at the University of Michigan Medical Center, Ann Arbor, in an attempt to correlate eventual treatment results with the degree of denial or change in degree of denial. The subjects were 100 male "veterans" (mean age 31.8 years and average duration of alcoholism 10 years) and they were treated psychotherapeutically in an open ward unit for an average period of 162 days. Follow-up data for an average period of 42 months after discharge were available in 91

At the end of this period 14 patients were rated as improved, 21 slightly improved, and 33 unimproved; of the others, 9 were lost to follow-up, 9 were in prison, 7 in hospital, and 7 were dead. The degree of denial was rated on a 5-point scale (0 to 4), the rating of 4 being a poor prognostic sign, since of the 33 men so rated only one improved significantly. It was observed that the unimproved group had a consistently high rating of denial, whereas the 35 patients who improved showed much lower rating. The authors note that while the level of denial on admission has some significance, a more important prognostic point is the relative rigidity or flexibility of this defence mechanism. They therefore conclude that this study confirms that denial is a significant part of the syndrome of alcoholism, and it is the capacity to decrease denial that is of significance for a favourable prognosis. N. Rethod

1493. Integrated Drug- and Psychotherapy in the Treatment of Alcoholism

G. S. BECKER and P. ISRAEL. Quarterly Journal of Studies on Alcohol [Quart. J. Stud. Alcohol] 22, 610-633, Dec., 1961. 13 refs.

In the last few years it has become increasingly clear that in the psychotherapeutic management of the alcoholic certain modifications of conventional techniques are necessary. The authors report a study in which psychotherapy was combined with drug therapy, the aim being to determine whether this integrated approach would clarify some of the operative factors of this kind

of treatment. The drugs were 200 mg, of meprobamate outly of as a result of admission to hospital, and suggest sule and the subjects were an uncontrolled series of 38 seeking to make a case for the efficacy of a new drug. alcoholic out-patients (30 men and 8 women, average age 43 years). Medication, which was maintained for one year, was given for four main symptoms: _tension, insomnia, anxiety, and the "hang-over" syndrome. Unpleasant side-effects occurred in only one case.

The authors found that this medication had a definite symbolic meaning to the alcoholic, and therefore the method of administration had to be suited to the patient's stage in psychotherapy. To alcoholic patients who had neither the inclination nor capacity to endure psychic discomfort the capsule represented immediate relief. similar to that obtained from alcohol. It was apparent that the placebo effect played an indeterminate part. As treatment progressed the patient was led to an understanding of the dynamic meaning of the drugs. The authors conclude that this integrated form of psychotherapy is applicable to a wide range of problems in which an imperative need for quick relief of tension interferes with the establishment and maintenance of a psychotherapeutic relationship. , N. Rathod ,

AFFECTIVE DISORDERS

1494. Adjunctive Therapy in Depression; a Controlled Trial of Nialamide

J. W. AFFLECK, A. D. FORREST, and F. M. MARTIN. Journal of Mental Science [J. ment. Sci.] 107, 997-999, Nov., 1961 [received Jan., 1962]. 5 refs.

In this study 50 out of 68 severely depressed patients (33 women and 17 men) admitted consecutively to the Royal Edinburgh/Hospital were selected for a doubleblind trial of nialamide, a hydrazine in the amine-oxidase inhibitor group. The majority (26) were aged between 46 and 65 years. The patients, divided at random into two groups, received either 50 mg. of nialamide or 50 mg. of chlorpromazine three times a day, the tablets being of identical appearance. Their condition was rated on a 16-item, 5-point scale before and again 2 weeks after the beginning of treatment. Patients who then showed a significant improvement were given known nialamide; 50 mg. 3 times daily, and re-assessed at 4 weeks, those who failed to improve receiving other appropriate treatment.

At the end of 2 weeks, of the 6 men and 20 women given : nialamide, 20 (76.9%) had improved, compared with 16 (66.6%) of the 11 men and 13 women given chlorpromazine. After 4 weeks, 13 patients (50%) had recovered with nialamide and 10 (42%) with chlorpromazine. At neither time, however, was the difference between results in the two treatment groups statistically significant, and the authors consider that further follow-up is required. They point out the difficulties in defining the type of case dealt with in a trial of this type despite the availability of extensive catamnestic data: Indeed, the more extensive the investigation, the more blurred do initial differences often become. They also emphasize the frequency with which depressive illnesses remit, either spontane-

and 25 mg, of promazine hydrochloride in a single cap-; that these facts are sometimes conveniently forgotten in Alan A. Black

> 1495. Comparison of Two Anti-depressant Drugs (Imipramine and Pheniprazine) in Endogenous Depressive IIInesses in Female In-patients.

D. P. OAKLEY. Journal of Mental Science [J. ment. Sci.] 107, 1000-1002, Nov., 1961 [received Jan., 1962]. 2 refs.

During a one-year period 59 women aged between 38 and 75 (mean 56.5) years suffering from endogenous depression were admitted to Whittingham Hospital, Preston, Lancs. As 10 of these patients had already started treatment with one or other of the drugs under consideration only 49 patients qualified for the trial, which was conducted "blind". They were divided at random into two groups, 26 receiving imipramine ("tofranil") and 23 pheniprazine ("cavodil"), both drugs being given over a fixed, currently acceptable, dose range. All the patients were seen by the author before treatment and at weekly intervals for 4 weeks, and on each occasion were rated on 10 variables, using a 3-point scale. No significant differences between the two methods of treatment emerged; thus at 4 weeks 14 out of 26 patients-(54%) given imipramine had recovered, compared with 13 out of 23 (57%) receiving pheniprazine. Further Alan A. Black follow-up was not practicable.

1496. Phenelzine and Dexamphetamine in Depressive Illness: a Comparative Trial.

E. H. HARE, J. DOMINIAN, and L. SHARPE. British Medical Journal [Brit. med. J.] 1, 9-12, Jan. 6, 1962. 3 figs., 5 refs. .

This paper from the Bethlem Royal and Maudsley Hospitals, London, reports a controlled comparative trial of phenelzine, dexamphetamine sulphate, and a placebo (lactose) in the treatment of depressive illness of moderate severity. Of the 46 patients admitted to the trial 31 females and 12 males (median age 42) completed it! The drugs (phenelzine 30 mg. and dexamphetamine sulphate 5 mg.) and the lactose were made up in tablets identical in appearance and given twice daily at 10 a.m.: and 3 p.m. from Monday to Friday of each week for 2 weeks in random order of administration known only to the pharmacist. Each patient was assessed by the same observer on entry to the trial and at the end of each 2-week period on a 5-point scale to rate the intensity of ... depression, retardation, agitation, anxiety, hypochondria, anorexia, and insomnia. The ratings for these 7 features made by a second observer were compared for 34 of the cases. The observers were agreed on the direction of the change in regard to agitation in 74% of cases, depression in 64%, and anxiety in 40%. \Only in the case of anxiety were their views ever directly opposed on the question of whether the patient was better on one drug than another, and this occurred in only 7 of a possible 82 comparisons.

In their effect on depression neither phenelzine or dexamphetamine was significantly better than each other or than lactose. In its effect on agitation and anxiety phenelzine was significantly better than both lactose and

dexamphetamine, the two last showing no significant difference between each other. In none of the other clinical manifestations assessed was there any significant difference between the 3 forms of therapy. The authors conclude that dexamphetamine does not appear to be an effective antidepressive drug [it should be noted that only 5 mg. twice daily was given] and that any effect phenelzine has is as a sedative and not as an antidepressant. They suggest that a similar controlled comparison of phenelzine and a sedative should be carried out. They note the spontaneous improvement of depression during the trial'(70% at the end of 6 weeks), a finding which emphasizes the need for very carefully controlled trials such as this in assessing the efficacy of drugs in the treatment of depressive illness. Christopher Wardle

SCHIZOPHRENIA

1497. The Relationship between Thyroid Function, Clinical Course, and Therapeutic Response in Schizophrenia. (Die Beziehungen zwischen Schilddrüsenfunktion, Verlaufsform und Therapieprognose bei der Schizophrenie) H. VON BRAUCHTISCH. Archiv für Psychiatrie und Nervenkrankheiten [Arch. Psychiat. Nervenkr.] 202, 331-345, 1961. 9 refs.

A relationship between thyroid dysfunction and schizophrenia has long been suspected and although the two conditions are of independent aetiology, the state of thyroid function has been shown to have some bearing on certain aspects of schizophrenic illnesses. From among 235 psychiatric patients under treatment at the University Psychiatric Clinic, Zürich, 97 were selected in whom the diagnosis of schizophrenia could be established beyond doubt and in whom follow-up studies could readily be carried out. These patients were assessed as being hyperthyroid, hypothyroid, or euthyroid on the basis of the clinical findings, supplemented by radioactive iodine and other biochemical investigations.

The following correlations were found to exist. male schizophrenics showed thyroid dysfunction more frequently than males, as also did persons of pyknic build of both sexes than those of other body types, patients of athletic build showing the fewest thyroid abnormalities. In young patients thyroid dysfunction was more frequent than in old ones, and in fact the negative correlation between increasing age and thyroid dysfunction was almost linear. Low intelligence and propfschizophrenia" was found more frequently in the patients' with hypothyroidism-possibly a link with cretinism? Of the clinical subgroups, the catatonic patients were most often hyperthyroid and the paranoid schizophrenics most often hypothyroid. The course of the schizophrenic illness was directly related to thyroid function in that the higher the thyroid activity, the more the schizophrenia tended to show spontaneous remissions; but the predicted low thyroid function in end-states could not be demonstrated, nor was any other correlation found between the patient's end-state and thyroid function. An acute onset was shown to correlate with hyperthyroidism, while a good response to neuroleptic drugs also depended to a certain extent on thyroid function, though no such correlation was found with other forms of treatment.

[Although in this study the author speaks of "correlation" neither the statistical methods employed nor the index of significance are stated, only the crude figures being presented.]

J. Hoenig

1498. Disturbances of Glucose Metabolism in Schizophrenia. (Perturbations du métabolisme du glucose chez les schizophrènes)

M. JAROSZ. Annales médico-psychologiques [Ann. méd.-psychol.] 119, 633-650, Nov., 1961 [received Jan., 1962]. 3 figs., 35 refs.

Glucose metabolism was studied at the Psychiatric Clinic of the Academy of Lodz, Poland, in 14 male and 11 female schizophrenic patients aged 20 to 33 years with a duration of illness ranging from 2 months to 5 years; hospital staff of comparable age and sex served as a control group. The physical state of the patients, assessed clinically and by laboratory investigations, was found to be normal. Except for 6 patients who received small doses of chlorpromazine, no subject received drugs during the investigation, in which glucose was administered in the fasting state either orally or by two intravenous injections separated by an interval of 10 to 20 m nutes. Blood glucose levels were determined at zero time and thereafter at frequent intervals up to 3 hours. In another. series of experiments blood glucose levels were determined after the intravenous injection of insulin without administration of glucose.

Mean values (with standard errors) for the essential features of the blood glucose curves are given for each group. The results indicated a lower than normal tolerance for glocose in schizophrenic patients, which improved after a period of treatment [the latter is not precisely specified, but apparently took diverse forms]. In the glucose tolerance experiments levels of significance (with P<0.001) were found for the difference between untreated patients and normal subjects. Individual variation, however, was greater in the patients, particularly before treatment.

R. Rodright

1499. Falsification of Bodily Needs and Body Concept in Schizophrenia

H. BRUCH. Archives of General Psychiatry [Arca. gen. Psychiat.] 6, 18-24, Jan., 1962. 12 refs.

The author reports from the College of Physicians and Surgeons, Columbia University, New York, her deductions on the development of an abnormal body image in schizophrenics. Her views derive from her own work as a psychiatrist and psychoanalyst and are discussed in the light of recent work in other fields of psychology.

The term "body concept" proposed by Kolb is used to include sensations from inside the body in an extended concept of the body image. Traditional psychoanelytical formulations of the infant's learning to feel itself a separate being are said to overlook the fact that the infant is not wholly dependent. It signals its needs, and the responses made to these signals are crucial to the infant's learning to identify its inner sensations correctly. When

the child expresses a need then, if the environment fails to provide the appropriate response but errs by being neglectful or over-solicitous, or in other ways, the child may misinterpret its original sensation or be confused about its meaning and grow up submissive to environmental demands or in an equally stereotyped negativism, in either case without basing action on its own inner needs. Support for this view is found by the author in Harlow's description of the "non-social syndrome" in monkeys reared on dummies instead of mothers; it is suggested that their inadequacies result from their not having had the chance to learn adaptive behaviour.

Two case histories are cited, both with severe eating disorder. They illustrate how a disturbed human parent will handle her child in terms of her own feelings, warping the child's development, rather than meet the needs the child is feeling and which a relaxed and loving mother would sense.

It is concluded that awareness of bodily sensations and of self-initiated thought and action must be present to the patient or evoked for successful treatment.

R. P. M. Urquhart

TREATMENT_

1500. Methylphenidate Given Intravenously as an Aid to Psychotherapy

F. HOCKING. Medical Journal of Australia [Med. J. Aust.] 1, 77-80, Jan. 20, 1962. 31 refs.

After a short historical survey of the use of drugs to "loosen the patient's tongue" and so assist psychotherapy the author reports his experience with the piperidine derivative methylphenidate ("ritalin") given intravenously. This drug is a mild antidepressant, stimulating the central nervous system probably at both cortical and subcortical levels and producing only a slight increase in blood pressure and pulse rate. There is no evidence that it causes impairment of hepatic, renal, or bone-marrow function. Side-effects are restlessness, tachycardia, shortness of breath, and increased psychomotor activity, but these are seldom severe. In the present study methylphenidate was given intravenously, 20 mg. in 10 ml. of sterile water, to 30 patients suffering variously from chronic anxiety, tension, conversion neuroses, reactive depression, and in one case a paranoid state.

During treatment most of the patients reported a sense of well-being and relaxation. The drug helped most of them to talk more freely and gave an objective degree of "ventilation" of thoughts and feelings in 20 cases. In one case there was a severe abreaction, but this patient had a history of sensitivity to many other drugs. Later, to 24 of these patients both methylphenidate and amylobarbitone sodium were given for comparison. No patient talked more freely after receiving amylobarbitone than after methylphenidate. Combination of the two drugs did not give better results than did methylphenidate alone, except that some of the side-effects of methylphenidate were prevented by simultaneous administration of sodium amytal. No untoward effects followed the administration of methylphenidate after sodium amytal E. H. Johnson in this series.

1501. Hallucinations, Delusions, and Ideas of Reference Treated with Psychotherapy

S. ARIETI. American Journal of Psychotherapy [Amer. J. Psychother.] 16, 52-60, Jan., 1962. 18 refs.

The author has found that in some cases of schizophrenia, as soon as a working relationship with the patient has been established, interpretations can be given which provoke insight into the circumstances in which symptoms may appear. Thus a patient who hears hallucinatory voices of neighbours deriding him may be taught to see that the voices occur when he is thinking about and expecting to hear people talking against him. Patients who hotly deny ideas expressed by their "voices" (for example, that they are bad or sinful) may be led to realize that at times in the past they may have held such selfdisparaging opinions. Similarly, patients who misinterpret casual happenings as signs of a plot against them may be brought to understand that their symptoms serve to corroborate a pre-existing mood during which they were looking out for unfavourable signs. Recognition of the emotional attitude which precedes the symptoms is the first step in learning control over them.

Another technique exploits the partial reality basis of some delusions. For example, a patient complained of a friend who when visiting her brought along a pet dog: "You see! She thinks my home is a dog house. She thinks I am a dog." This example of concrete thinking was based upon a feeling that the friend was domineering and treated people like dogs. The patient was therefore complimented for astuteness in recognizing the friend's true attitude. The effect of such an interpretation is to increase rapport, since the patient thinks his feelings are being understood. He is then encouraged to tackle the situation realistically. D. J. West

1502. Atropine Premedication for Electric Convulsion Therapy

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A. J. CLEMENT. British Medical Journal [Brit. med. J.] 1, 228-229, Jan. 27, 1962. 1 fig., 6 refs.

A comparative study of two routes of atropine premedication in patients undergoing electric convulsion therapy (E.C.T.) is reported from St. Thomas's Hospital, London. One group of 100 patients received 1 mg. of atropine subcutaneously half-an-hour before E.C.T. while another group of 100 received the same dose of atropine intravenously 75 seconds before treatment. The pulse rate and apex beats were recorded. In 22 of the patients given, atropine subcutaneously there was complete disappearance of heart sounds and pulse for 1 to 5 seconds after the shock. This occurred in only one of the patients given atropine intravenously; another patient in this group had severe bradycardia for 5 seconds.

The author refers to an investigation by Barlow (described in a personal communication in 1961) of the effect of E.C.T. in atropinized and non-atropinized patients. This showed that there was a gross fall in blood pressure lasting 5 seconds in the latter group, whereas there was "virtually no change" in the patients who had received atropine intravenously. It is suggested that 1 mg, of atropine intravenously will provide a far better yagal block than 1 mg, subcutaneously and that

injection 75 seconds before the shock will ensure maximum effect. It is noted that the one patient in the present series in whom there was a short cessation of pulse in spite of atropine intravenously received E.C.T. only 45 seconds afterwards, before full vagal block developed.

E. H. Johnson

1503. Controlled Multifocal Frontal Leucotomy for Psychiatric Illness

H. J. CROW, R. COOPER, and D. G. PHILLIPS. Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat:] 24, 353-360, Nov., 1961. 5 figs., 17 refs.

A method has been developed for obtaining greater precision in the control of the site, size, and duration of lesions in frontal leucotomy. It involves the introduction of large numbers of small, chronically indwelling, gold intracerebral electrodes in the frontal lobes. A temporary leucotomy can be achieved by electrical polarization of these electrodes; where relief is obtained a permanent selective leucotomy can be performed by electro-coagulation using direct current.

The results in the first five cases are briefly described. The effects of the procedure can be observed while the patients are leading a normal life as well as in hospital. No difficulties have been encountered with infection, insertion trauma, or electrode reaction. The patients tolerate the implantation well for periods of several months.—[Authors' summary.]

1504. Deconditioning and Time-therapy

G. DE M. RUDOLF: Journal of Mental Science [J. ment. Sci.] 107, 1097-1101, Nov. 1961 [received Jan., 1962]. 8 refs.

In view of the recent revival of interest in deconditioning the author describes a hitherto unreported study which was carried out 20 years ago in Plymouth during the many enemy air raids on that town. He enumerates five types of conditioning therapy and describes examples of three of these, namely, positive conditioning, conditioned inhibition; and reciprocal inhibition. The subjects of the study were 35 soldiers who were referred by medical officers on account of objective signs of excessive anxiety. The deconditioning treatment consisted in exposing the men to the stimuli which had given rise to the anxiety, namely danger, during further air raids. Notes were taken of objective signs of anxiety, such as tremor, weeping, standing in a corner, or lying under the bed during the raid. A few patients showed less fear progressively as the number of raids increased. Conditioned inhibition was seen in one man in whom three raids a day over some days had given rise to his fear. When the frequency of the raids decreased he showed no sign of fear, but was again fearful when they became more frequent. Reciprocal inhibition was thought to have operated in one man who usually went downstairs in a raid and still showed fear, but who after once staying upstairs, considered more dangerous and antagonistic to anxiety, showed no further symptoms. Other cases described showed that symptoms due to fear can cease, without treatment, with the passage of time. Of

the 35 patients undergoing repeated stimuli none got worse, and 16 improved. The only additional treatment given was the occasional administration of a hypnotic drug.

J. S. Bearcroft

1505. An Examination of the Mechanism of Therapeutic Action of Certain Psychotropic Substances by Experimental Investigation of Conditioned Reflexes. (Сценка механизма терапевтического действия нексторых психотропных веществ при экспериментальном исследовании условных рефлексов)

A. Jus. Журнал Невропатолсгии и Психиатрии [Zh. Nevropat. Psihiat.] 61, 1828-1835, No. 12, 1961. 7 figs., 13 refs.

This paper from the Psychiatric Clinic of the Medical Academy, Warsaw, describes an investigation conducted over the past 10 years of the conditioned reflex activity in patients suffering from schizophrenia, manic-depressive psychosis, involutional psychosis; post-traumatic psychosis, and psychoneurosis, and treated variously with insulin coma, chlorpromazine, reserpine, "majeptil", "haloperidol", and nialamide. The investigation was in two parts, the first being on a group of schizophrenics who were treated by insulin coma. By substitution of a placebo it was shown that the psychic, neurological, and biochemical aspects of hypoglycaemia became conditioned to various external factors. The presence of this conditioning in well developed form was a favourable prognostic sign and its absence was unfavourable.

In the second part of the investigation the reactivity of patients was studied by the simultaneous recording of the electroencephalogram (EEG), electromyogram, psychogalvanic reflex, and motor movements. It was possible to establish conditioned blocking of the α-rhythm in the EEG to sound stimuli, a conditioned tonic electromyographic reaction to auditory and visual stimuli, and conditioned overt motor reflexes also to auditory and visual stimuli. In patients in a state of catatonic stupor treated with insulin or neuroleptic drugs and in those with other psychotic illnesses such as depressive states the appearance and strengthening of conditioned reflexes proceeded in parallel with recovery. In paranoid syndromes and involutional psychoses the ability to differentiate two similar stimuli proved an important sign of recovery. Sometimes the presence of certain reflexes inthe absence of others was a favourable sign. However, in simple schizophrenia improvement in the clinical state showed little relation to changes in the conditionedreflexes probably, it is thought, largely owing to the inadequacy of present methods of investigation.

The author ends by speculating on the mode of action of certain drugs and the mechanism of the various psychic disturbances. Chlorpromazine may lower the bio-electric activity of the cerebral cortex and also cause changes in the interrelationship between functional states of the mid-brain, the thalamus, and the reticular formation. It is considered that these experiments reflect the bio-electric picture of attention and its changes under the influence of the neuroleptic drug. Certain forms of catatonic stupor were thought to display a disturbance of perception.

G. P. McGovern:

Dermatology

1506. Psychophysiological Mechanisms in Skin Diseases H. C. Bethune and C. B. Kidd. Lancet [Lancet] 2, 1419-1422, Dec., 30, 1961. 34 refs.

This paper from the University of Edinburgh formulates a heuristic concept to explain the mechanisms by which psychological stress can produce specific physiological or pathological changes in the skin. After a brief review of some traditional views as well as more recent concepts, the authors stress the importance of suggestion [without, however, offering any definition of this term] as the common factor in explaining the success of different therapeutic approaches. They approve of the explanation of a psychosomatic effect in terms of reaction to a state of "high drive" or as a consequence of a learnt response, and cite experimental findings in support. There is here a similarity to the physiological changes in hypnosis, and induced "ideomotor action" could well produce the postulated high drive. More complex changes can, on the same principle, be brought about in areas under autonomic control.

Three components are postulated in these experimentally induced psychophysiological phenomena: (1) a state of emotional high drive, which initiates activity of the central nervous system; (2) the subjective feeling of the physiological response directs nerve impulses to the organ or other seat of the sensation and this initiates "ideovisceral" or "ideovascular" action; which (3) is reinforced by an afferent "feed-back" mechanism. A constitutional factor [so often invoked to explain the difficult problem of organ selection] of "organ inferiority" would potentiate these mechanisms because the patient has "learned" to become conscious of subjective feelings there. In some cases continued high drive produces changes of such an order that suggestive therapy is bound to fail. Case histories are presented to support these theories; in these cases the treatment included suggestion, induced perceptual distortion, and redirection of drive.

The authors conclude that "the psychological treatment of skin diseases based on this concept makes possible considerable physiological readjustments, and it may explain the success or failure of treatment by a variety of psychological therapeutic approaches".

F. E. Kenyon

1507. Atopic Eczema in European and Negro West Indian Infants in London

L. R. DAVIS, R. H. MARTEN, and I. SARKANY. British Journal of Dermatology [Brit. J. Derm.] 73, 410-414, Nov., 1961. 3 refs.

This paper from the Belgrave Hospital for Children (King's College Hospital), London, reports a comparative study of atopic eczema as seen during the past year in 50 European and 44 West Indian infants under 2 years of age. It is notable that of all infants under 2 years

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suffering from atopic eczema 40% were West Indian, whereas only 9% of those attending the casualty department and 10·2% attending for haematological investigation at the hospital were West Indians. This high incidence of atopic eczema among West Indians. This high incidence of atopic eczema among West Indian children living in London is even more striking when considered with a report of only 39 cases being recorded at the University College Hospital of the West Indias between 1952 and 1959, suggesting that the prevalence of the disease is much greater in such infants in London. Of the 50 European children, a family history of atopy was obtained in 32 (64%), but only in 3 (7·5%) was there a similar family history in the West India patients.

Clinically, the time of onset and severity of the disease appeared to be similar in the two groups. Patches of hypo- and hyperpigmentation were more common in the West Indians and eruptions with closely set papules on the trunk were frequent. The incidence of ichthyosis was similar, but occasionally lichenification in the West Indian infants was striking in its extent. Haematological examination showed that an iron deficiency anaemia was twice as frequent in the West Indians. An eosinophilia was found in 50% compared with an incidence of 34% in the European children and the absolute numbers of eosinophil leucocytes also tended to be higher. Parasitic infection was excluded as a possible cause and the degree of eosinophilia bore no relationship to the severity of the eczema. In a control group of healthy infants of both nationalities the incidence of eosinophilia was found to be no greater in the West Indian than in the European infants.

Benjamin Schwartz

1508. The Mechanism of Contact Sensitisation. [Review Article]

H. O. SCHILD. Journal of Pharmacy and Pharmacology [J. Pharm. Pharmacol.] 14, 1-8, Jan., 1962. 48 refs.

1509. Treatment of Trophic Ulcers with an Oily Preparation of Carotene. (Лечение больных торфическими язвами масляным препаратом каротина)
М. А. Какадеzian, N. N. Antonik, and I. A. Ultima.

Вестник Дерматоловии и Венероловии [Vestn. Derm. Vener.] 36, 30-33, Jan., 1962. 4 figs.

It is considered that vitamin A increases the resistance of the organism to infection, and also contributes to normal cornification. For this reason the present authors employ carotene, which is a precursor of vitamin A, and has previously been used successfully in treating burns. During the past 2 years they have treated 43 patients suffering from trophic ulcers of the legs with local applications of carotene in soya oil in a concentration of 2,700 to 3,000 mg. of carotene per litre, simultaneously giving carotene by mouth. The ulcers treated were due to varicose veins, thrombophlebitis, x-irradiation, and tuber-

culosis. In 33 of the 37 patients who completed the course the ulcers healed in 8 to 28 days, and in 4 patients the treatment took longer. The scar tissue appeared to be very stable, since in several patients recurrences appeared at different sites, while the original scars remained whole. The authors consider this to be a physiological method of treatment.

N. Hopewell

1510. Histamine in Plasma in the Induced Urticaria Due to Cold. [In English]

I. Spužić and L. IVKOVIĆ. Acta allergologica [Acta allerg. (Kbh.)] 16, 228-231, 1961. 12 refs.

The authors of this paper from the Institute for Medical Research, Belgrade, describe a study of the part played by histamine in the development of urticaria due to cold. In 7 patients known to suffer from cold urticaria the plasma histamine level was determined immediately before and again 10 to 12 minutes after being washed in cold water at 10° C. A marked increase in the plasma histamine level was observed in only one patient; in the remaining 6 patients there was no immediate rise.

A. W. Frankland

1511. "Hedgehog Ringworm"

M. P. ENGLISH, C. D. EVANS, M. HEWITT, and R. P. WARIN. *British Medical Journal [Brit. med. J.]* 1, 149-151, Jan. 20, 1962. 1 fig., 3 refs.

Since 1958 ringworm contracted from hedgehogs has been diagnosed in 13 patients seen at Bristol General Hospital and the Royal Cornwall Infirmary, Truro. The fungus in question was an atypical strain of Trichophyton mentagrophytes with yellow pigmentation. In 2 instances the fungus isolated from the patients was the same as that isolated from the actual hedgehog which they had handled: in the other cases there was a history either of handling hedgehogs or of keeping dogs which were keen hedgehog hunters. The authors state that there is also evidence of the indirect transfer of this fungus to man by dogs. In 4 patients the eruption was suggestive of ringworm, but in the remaining 9 the appearances were very similar to those of eczema. In 4 of the latter group pustules were present which were thought to be due to secondary staphylococcal infection. It is suggested that in the past cases of infection with this fungus may have been misdiagnosed as eczema. Infection of the fingernails occurred in 2 patients.

The development of ringworm after contact with hedgehogs was first noted in New Zealand and it is interesting that hedgehogs were introduced into New Zealand from Britain in 1885.

P. T. Main

1512. Management of Pyogenic Cutaneous Infections J. W. Burnett. New England Journal of Medicine [New Engl. J. Med.] 266, 164-169, Jan. 25, 1962.

A double-blind trial is reported of the efficacy of erythromycin propionate in impetigo and in secondarily infected dermatoses in 89 patients seen at Johns Hopkins Hospital, Baltimore. Examination of a Gram-stained smear taken from beneath a crust was found to be the most useful procedure for determining the presence of infection.

The commonest organisms found were Staphylococcus aureus and β -haemolytic streptococci. The application of wet dressings did not influence the results. Cure was obtained in about 10 days with erythromycin compared with 25 days with a placebo. The lesions in 6 patients who did not respond to a 5-day course of erythromycin cleared promptly after a further period of treatment with the drug. In 2 patients in the series there was evidence of acute glomerulonephritis. Although the organisms were erythromycin-resistant in 3 cases the lesions nevertheless responded to treatment.

John T. Ingram

1513. Xeroderma Pigmentosum and Radioactive Phosphorus. (Xeroderma pigmentosum et phosphore radioactif)

F. PINET, A. VERAIN, C. BERAUD, and A. PINET. *Presse médicale* [*Presse méd.*] **69**, 2619–2622, Dec. 25, 1961. 9 figs., 1 ref.

Xeroderma pigmentosum, which is common in Algeria, usually begins its mutilating course in childhood and evolves continuously until the adult patient is reduced to a semi-permanent hospital existence, the victim of severe scarring. Observations on patients treated by electrocoagulation and radiotherapy at the Pierre and Marie Curie Centre, Algiers, demonstrated that in the areas of radiation atrophy no further tumours developed, and the authors therefore introduced, as a prophylactic measure, treatment with radioactive phosphorus (32P), which because of the superficial nature of its radiation causes no damage to the remaining normal skin. Dosage was calculated by means of a scintillation counter whose surface area was identical with that of the applicator, while a plastic montage was constructed to ensure the homogeneity of the irradiation. The applicator itself consisted of a 6-mm. "plexiglass" mould into which was poured the solution of 32P in heated gelatin and water. This was covered with 20 thicknesses of gauze and applied to the skin with a cotton bandage. Duration of application was calculated as the quotient of total dose divided by initial dose and was usually between 24 and 30 hours, with a consequent total dose cf 5,000

The expected radiation reaction was completed within 40 days, leaving an intact epidermis with some depigmentation. Central ulceration developed in a few areas, but this healed without complication and with no evidence of radiodermatitis. A few of the patients also developed a slight fever and anorexia between the 15th and 20th days of treatment, but again this cleared spontaneously. Of the 6 patients who received multiple treatment in this way none developed either general or local complications and, provided adequate areas of depigmentation were obtained at the treatment sites, no further neoplasms have, so far, appeared in these areas.

Allene Scott

1514. Some Aspects of the Biology of the Epidermis. (Malcolm Morris Memorial Lecture)

B. F. Russell. British Medical Journal [Brit. med. J.] 1, 815-820, March 24, 1962. Bibliography.

Paediatrics

1515. Plasma Volume Changes in the Neonate M. W. Steele. American Journal of Diseases of Children [Amer. J. Dis. Child.] 103,10-18, Jan., 1962. 16 refs.

Human serum-albumin-bound I¹³¹ was used to determine total body plasma volume at age 15 minutes and age 2 hours, 15 minutes, in 18 subjects, 9 of which were normal newborns and 9 of which were delivered by Cesarean section. From plasma volume and the packed cell volume, the red blood cell mass and total blood volume were calculated.

The reliability and accuracy of the I¹³¹-tagged albumin method for determining plasma volume was seen to be dependent on correction of certain errors. Adsorption of the reagent by the glassware used could be prevented by the addition of enough protein to the standard and injection solutions so as to keep the concentration of protein greater than 0.05 mg. per cc. Error due to excessive loss of free I¹³¹ from the vascular space could be minimized by using an optimum mixing time, which was 5 minutes in this study.

For a mean packed cell volume of 50.9% at age 15 minutes, the mean plasma volume was 44.5 cc. per kg., the mean red cell mass was 35.9 cc. per kg., and the mean total blood volume was 80.4 cc. per kg. Two hours later, for a mean packed cell volume of 54.9%, the mean plasma volume was 40.5 cc. per kg., the mean red cell mass was 37.0 cc. per kg., and the mean total volume was 77.5 cc. per kg. The mean loss of I¹³¹-tagged albumin from the vascular space-was 27.3% in 1.8 hours.

A statistically significant rise in packed cell volume was found in the first 2½ hours of life. This was shown to be accounted for solely by a shift of plasma out of the vascular space. There was no significant change in the red blood cell mass, so that, of necessity, there was a small change in the total blood volume. The degree and the direction of the plasma shift was dependent on the height of the initial blood or plasma volume. The higher the latter, the more plasma shifted out of the vascular space. If the initial blood or plasma volume was too low, plasma shifted into the vascular space.

It is suggested that the pathogenesis of hyaline membrane disease is the simultaneous occurrence of 2 physiological conditions: the aspiration of large amounts of amniotic fluid and the shift of large amounts of plasma into the pulmonary alveoli. It was further suggested that the disease could be prevented if the latter component were prevented by keeping the baby's blood volume at birth within the normal or low-normal range.—
[Author's summary.]

1516. "Early" Exchange Transfusion
W. WALKER. British Medical Journal [Brit. med. J.] 2,
1513-1516, Dec. 9, 1961. 2 figs., 3 refs.

When haemolytic disease of the newborn is very severe, exchange transfusion must be performed as soon as possible. In the majority of cases, however, the urgency

is not so great and treatment is often delayed for some hours until a time convenient to the operator. The author, at the University of Durham Medical School, has reviewed his records to see whether delay in starting treatment for 9 to 16 hours after birth was beneficial or harmful to the baby. The main object of exchange transfusion is to replace the baby's erythrocytes with donor cells which will not be haemolysed, and its efficacy may be judged by the subsequent levels of bilirubin and haemoglobin in the serum.

In general, if the infant's cord haemoglobin value was more than 11.5 g. per 100 ml. the need for exchange transfusion was not considered to be urgent and treatment was started at a convenient time of day. During 1958, 1959, and 1960, 80 such infants were treated between 9 and 24 hours after birth (67 of these between 9 and 16 hours) and 126 received treatment at 1 to 9 hours. Some selection of cases for earlier or later treatment was inevitable owing to various factors, and to obviate this, cases receiving early or late treatment were paired with regard to birth weight and the cord-blood haemoglobin and bilirubin values. A moderate degree of jaundice after treatment was more common in the babies who received treatment after 9 hours, but mild or severe jaundice occurred with equal frequency in both groups. Five infants in each group needed a second exchange transfusion, and 2 from each group required more than two. Seventeen infants required a simple transfusion for anaemia (haemoglobin less than 7.4 g. per 100 ml.) in the first 6 weeks of life, and 12 of these 'had received "early" treatment. The only 2 deaths in the series were attributed to congenital heart disease. Infants treated more than 9 hours after birth appeared to tolerate the exchange transfusion better than those treated early.

The author concludes that, if the cord-blood haemoglobin value exceeds 11.5 g. per 100 ml., in the absence of other evidence of severe haemolytic disease exchange transfusion may safely be delayed for up to 16 hours after birth.

F. P. Hudson

1517. Pyloric Stenosis: Selective Medical and Surgical Treatment: a Survey of Sixteen Years' Experience N. M. JACOBY. Lancet [Lancet] 1, 119-121, Jan. 20, 1962. 11 refs.

The author reports a series of 195 cases of congenital pyloric stenosis admitted to the Children's Hospital, Pembury, Kent, between September, 1944, and December, 1960, and given "selective treatment". He points out that unfortunately there has been no standardization of the medical treatment of this condition; for example, the dosage of atropine methyl nitrate recommended by different authors has varied by as much as 600%, and as a result, medical treatment has fallen unjustifiably into disrepute, whereas with correct selection for type of treatment much can be achieved. In his experience the

indications for surgical treatment are: (1) vomiting beginning in the 2nd week of life or earlier, and (2) severe dehydration; while the indications for medical treatment are: (1) vomiting beginning in the 4th week or later; and (2) vomiting continuous for 3 weeks or more before the infant is first seen, provided dehydration is not severe.

The contraindications to medical treatment are severe dehydration or haematemesis. In this series an undoubted pyloric tumour was palpable in all cases; the diagnosis was made radiologically in only 4 cases. The male:female ratio was 4:1, that is, lower than the usually reported ratio of 5:1.

Among the 101 cases treated medically there were only 10 failures (which later required operation) and one death (1%), while among the 104 cases treated surgically (including the 10 medical failures) there was again one death (0.96%). Thus the over-all mortality was 1.03%. The average stay in hospital was 12.1 days for the medically treated group and 11.2 days for the surgically treated. The medically treated infants were 8 oz. (227 g.) above birth weight on admission and the surgically treated 1 lb. (450 g.) below birth weight. It is considered that an infant weighing less on admission than at birth is not suitable for medical treatment. The main principles of , the latter are: (1) reduction in the volume of the feeds; and (2) administration of atropine methyl nitrate, 0.1 ml. of a 0.7% alcoholic solution, before 4 feeds on the first day and before 3 feeds on subsequent days. All surgically treated cases in the series were operated on personally by the author, local anaesthesia and a high midline incision being used. Lignocaine is believed to have caused convulsions in one child. Persistent postoperative vomiting occurred in 10% of these cases and lasted one to 3 days, but then disappeared spontaneously. The cause of this is unknown, but it is noteworthy that 5 of the 8 infants were under 2 weeks of age at the time of the operation; the author now treats such cases medically until the third week of life. The 2 deaths in the series occurred in one child treated surgically who died of gastro-enteritis in 1946 and in one treated medically who was premature and died suddenly shortly after admission. Andrew M. Desmond

1518. Pyloric Stenosis: Postoperative Roentgen Studies and Their Clinical Significance

H. C. BISHOP and J. W. HOPE. Journal of Pediatrics [J. Pediat.] 60, 62-68, Jan., 1962. 10 figs., 5 refs.

Each year several children are transferred to the Children's Hospital of Philadelphia who have undergone pyloromyomectomy elsewhere but continue to vomit. Radiographic studies of these infants demonstrate that the pyloric canal still remains narrow, suggesting that an inadequate operation has been performed. In spite of this, however, most of these infants recover without recourse to a further operation. For this reason the authors considered it desirable to study the postoperative x-ray appearance of the pyloric canal in a series of their own cases. They therefore selected at random 20 infants (14 male, 6 female) on whom barium gastro-intestinal studies were performed at periods varying from the 2nd postoperative day to 6 months after opera-

tion. The appearances in preoperative radiographs are described for comparison.

The conclusions are that all infants studied radiographically following pyloromyomectomy show persistent abnormalities of the pylorus and the pyloric canal. Early studies within a few days of the operation present in most cases the same findings seen preoperatively, that is, a narrow, elongated pyloric canal and indentation of the duodenal bulb by the hypertrophied muscle mass. In spite of this, gastric emptying time is usually improved and as time passes the pyloric canal gradually shortens' and widens, the widening occurring first at the proximal end. The invagination into the proximal duodenum, however, usually persists for several months, suggesting that the muscular hypertrophy diminishes only gradually after operation. No firm correlation between clinical improvement and x-ray appearances was noted. Several infants who had not vomited postoperatively still showed a narrow pyloric canal, whereas some of those who did vomit more than usual postoperatively had the widest pyloric canals. This suggests that the operation is successful for some other reason than the merely mechanical effect of the myotomy, and it is postulated that this factor may be the division of encircling nerve filaments. during the operation, thus reducing spasm.

The importance of this investigation is that persistent vomiting following the Fredet-Ramstedt procedure should be treated medically rather than that a revision of the operation should be carried out; and that in such cases radiological studies, although interesting, are unlikely to be of significant help. Andrew M. Desmond

1519. Acute Renal Insufficiency in Infancy. (Insuficiencia renal aguda en el lactante)

H. Z. Macera, R. Meroni, R. Landivar, L. Marquez, L. Stigol, C. Cambiano, J. Bonduel, P. Garrahan, and J. L. Monserrat. *Prensa médica argentina [Pren. méd. argent.*] 48, 1617–1634, June 16, 1961 [received Feb., 1962]. 15 figs.

The paper begins with a résumé of the present know-ledge of the physiology and pathology of acute renal insufficiency in infancy, and 4 such cases are then described in detail. Diagnosis and prognosis depend largely on the results of renal puncture biopsy examination. Repeated punctures can show the recovery, establishment, or progress of the lesions independently of the clinical picture. It is important to be able to recognize the normal appearance of glomerular maturation to avoid diagnostic errors. Renal biopsy demonstrates the great capacity for structural recovery in the infant kidney.

Treatment depends on the cause of the condition. One group of patients consists of infants suffering from an obstruction in the urinary tract or from severe cehydration or shock, and here the primary cause must be remedied. A second group consists of those suffering from acute tubular necrosis as a result of trauma, toxaemia, or administration of sulphonamides, while in a third group there may be acute pyelonephritis or other renal lesions. [A good review of renal insufficiency in infants.]

J. G. Jarnieson

Medical Genetics

1520. A Sex-linked Blood Group
J. D. Mann, A. Cahan, A. G. Gelb, N. Fisher, J. Hamper, P. Tippett, R. Sanger, and R. R. Race, Lancet [Lancet] 1, 8-10, Jan. 6, 1962. 1 fig.

Hitherto, all human blood group antigens so far discovered have behaved as autosomal characters. This combined report from the Butterworth Hospital, Grand. Rapids, Michigan, and the Lister Institute, London, is the first to describe a sex-linked blood group, the gene for which, Xg^a, is carried on the X chromosome. The antibody, anti-Xg^a, which requires special antiglobulin serum for its detection, was found in a man aged 50 who had received many blood transfusions because of bleeding associated with familial telangiectasia.

Tests on the erythrocytes from 342 random Caucasians (154 males and 188 females) showed that 88.83% of the females were positive and 61.69% of the males; this difference is "overwhelmingly significant" ($\chi^2=34.8$ for 1 d.f.). Also a study of 50 families confirmed that the gene is on the X chromosome, in that: $Xg(a+) \times Xg(a+)$ matings (30 families, 64 children) only produced Xg(a+) daughters and only the sons were Xg(a-); in Xg(a+)male × Xg(a-) female matings (3 families with 7 children) all the sons were Xg(a-) and all the daughters Xg(a+); while in Xg(a-) male $\times Xg(a+)$ female matings (16 families with 30 children) offspring of any type were found. The corollary to these findings is that: of positive normal men the mothers and daughters must be positive, while of negative normal women the fathers and sons must be negative.

The finding of anti-Xg^a (unfortunately only one example so far) lays the foundation for plotting the X chromosome in man. Studies on red-green colour blindness, glucose-6-phosphate dehydrogenase deficiency, and haemophilia have already started. Investigations of Turner's syndrome (XO) and Klinefelter's syndrome (XXY) may also produce very interesting results.

I. Dunsford

1521. The Carrier State in Hemophilia A
J. H. Githens and P. J. Wilcox. Journal of Pediatrics
[J. Pediat.] 60, 77-83, Jan., 1962. 2 figs., 41 refs.

The authors report from the Universities of Kentucky and Colorado attempts to detect the heterozygous carrier state in haemophilia A (classified haemophilia) by the relatively simple method of adding small amounts of the carrier plasma in the thromboplastin generation test of the affected male in the family. The thromboplastin generation test was performed by a modification of the method of Biggs and MacFarlane. The plasma of 6 of 14 mothers (all but 2 known to be carriers) and 5 of 17 sisters gave poor correction of the plasma thromboplastin generation test. Thus the method appears to be as sensitive as many of the more complicated assay methods of antihaemophilic globulin. C. O. Carter

1522. A Genetic Study of Hereditary Renal Dysfunction with Associated Nerve Deafness

M. M. COHEN, G. CASSADY, and B. L. HANNA. American Journal of Human Genetics [Amer. J. hum. Genet.] 13, 379–389, Dec., 1961. 5 figs., 26 refs.

The authors report from the U.S. National Institutes of Health, Bethesda, Maryland, 5 families showing the syndrome of hereditary renal dysfunction with associated nerve deafness, the mode of inheritance of which has remained in doubt. A total of 339 individuals in 4 generations of these families were classified on the basis of clinical examination and/or clinical records. The familial distributions appeared to be inconsistent with inheritance as a partially sex-linked dominant or an autosomal dominant with a classic Mendelian segregation ratio, as has been previously proposed. It is suggested that the anomalous familial distribution could be explained if there were non-random chromosome segregation at the first meiotic division of gametogenesis together with preferential association of the autosome carrying the gene with the X chromosome.

H. Harris

1523. Familial Mongolism with Chromosomal Translocation Also Observed in Normal Boy Member. [In English]

O. LEHMANN and H. A. FORSSMAN. Acta paediatrica [Acta paediat. (Uppsala)] 51, 6-12, Jan. [received March], 1962. 4 figs., 15 refs.

1524. Risk of Dual Occurrence of Mongolism in Sibships J. M. BERG and B. H. KIRMAN. Archives of Disease in Childhood [Arch. Dis. Childh.] 36, 645-648, Dec., 1961. 14 refs.

The authors of this paper from the Fountain Hospital, London, have made a prospective follow-up of 367 children born to mothers who had previously given birth to a mongol child. The series was collected from two mental deficiency institutions, one in London and one in Surrey, and from the records of the four district offices of the London County Council. The information concerning the families was collected by social workers who visited the homes as a routine, noting particularly if there were other retarded children in the family. Of the 367 children 7 were reported to be mongols. authors state that the expected number for a random group of mothers of the same age distribution is 1.9. The observed finding of 7 is significantly higher than the expected, with a probability of 0.003. The data further suggest that there is a greater increased risk at younger maternal ages.

The series also included 9 pairs of twins, 6 of like sex, one pair being concordant for mongolism, and 3 of opposite sex, all discordant for mongolism.

C. O. Carter .

Public Health and Industrial Medicine

1525. Problems of Postvaccinal Encephalitis. (Probleme der postvakzinalen Enzephalitis)

A. HERRLICH. Deutsche medizinische Wochenschrift [Dtsch. med. Wschr.] 87, 71-76, Jan. 12, 1962. 21 refs.

Writing from the Bavarian Vaccination Centre. Munich, the author first discusses the reliability of the available statistics regarding the incidence of encephalitis following smallpox vaccination and points out that a number of forms of encephalitis are attributed to vaccination on doubtful grounds. The relationship between the encephalopathies of childhood (mean incubation period 8.6 days) and extensive focal perivascular encephalitis (mean incubation period 12.3 days) as representing a different response due to age is discussed, but the author concludes that only post-mortem studies can give reliable figures. The incidence in Bavaria of postvaccinal encephalitis after primary vaccination against smallpox for the period 1925-9 was 1 in 8,900, the total number of primary vaccinations being 1,024,479. In regard to prophylaxis, primary vaccination is recommended at age 4 to 6 months, passive immunity derived from the mother being considered sufficient protection up to that age. Of the total number of vaccinations mentioned above, 20% did not "take", but the response to subsequent vaccination was similar to that of a revaccination. Vaccination of a pregnant mother is not recommended because of possible foetal damage. Vaccination of the newborn has been found to be accompanied by only slight reactions. To reduce complications in older persons hyperimmune serum and gamma globulin are given as a routine. As a result complications have been fewer and it is suggested that a still higher dosage could prevent all reactions.

The possibility of using animal sera is also discussed. and work on an inactivated vaccine grown on calf embryonic muscle cells is described. Given subcutaneously or intradermally this produced local swelling and redness in 24 hours, which was considered to be due to an existing immunity; reaction did not mean absence of immunity. Serological studies indicated a response in 2 to 8 weeks; subsequently it was found that aluminium hydroxide was a suitable adjuvant. Immunization with antigen, followed 8 to 14 days later by vaccination, gave a better antibody response, the local lesion then showing the appearance of a revaccination. Out of a series of 423 patients so treated only 16 gave some side-reactions, these including fleeting rashes, a large local lesion, and pyrexia. It was thought that this might have been due to sensitivity to the culture medium. These reactions were reduced when sedation was combined with 1 to 2 ml. of (postvaccinal) gamma globulin given at the time of vaccination.

Experiments on monkeys clearly demonstrated that the best protection was given by a combination of antigen and vaccination. The author states that among 10,000 patients given this combined vaccination there has as yet been no case of encephalitis. (Unfortunately detailed results are not available.) It is suggested that the protection conferred by the antigen may not be a "real" immunity, but an altered immunity which prevents postvaccinal encephalitis.

[Further large-scale results should be of great interest, since with the reduction in the incidence of smallpox and the decline in routine vaccination in infancy, problems of primary vaccination in adults will certainly assume greater importance.]

Kurt Schvarz

1526. Persistence of Antibody following Booster Dose of Poliomyelitis Vaccine

R. J. Wilson, G. W. O. Moss, J. P. Jacobs, and D. R. E. MacLeod. Canadian Journal of Public Health [Canad. J. publ. Hlth] 53, 17-21, Jan., 1962. 3 figs., 11 refs.

At the Connaught Medical Research Laboratories, Toronto, neutralizing antibody to the 3 types of poliomyelitis virus in the serum of 54 children who had been vaccinated [presumably with Salk vaccine] was titrated after the primary course of vaccination, 2 weeks after a booster dose 11 months later, and again 18 and 36 months after that. In children who had had no antibody previously less antibody developed, and the rate of decline of the antibody was greater after the primary course of vaccination than in those who already possessed antibody as a result of natural infection. All these children developed antibody after the booster dose, and it reached the same level as in those with naturally acquired antibody.

The median antibody titre fell fourfold in the first 18 months following the booster dose and then fell a further twofold during the next 18 months. Of the children without naturally acquired antibody to a given type, 95% maintained measurable vaccine-induced antibody against that type for a 3-year period. It is estimated that the proportion would fall to 90% or less after 44 years. The authors therefore recommend that a second reinforcing dose of vaccine should be given 3 to 4 years after the booster dose to children who have received primary vaccination after the age of one year.

Janice Taverne

1527. Enteroviruses in Sewage and Epidemic Pollomyelitis in Eastern Canada

R. L. OZERE, R. FAULKNER, and C. E. van ROOYEN. Canadian Medical Association Journal [Canad. med. Ass. J.] 85, 1419–1424, Dec. 30, 1961. 17 refs.

Any future wide-scale use of oral poliomyelitis raccine might result in the virtual elimination of poliomyelitis viruses from the community. The appearance of wild virulent strains in communal sewage might herald a recrudescence of the disease. On this assumption the authors of this paper from Dalhousie University and

the Department of Public Health, Halifax, Nova Scotia, investigated some of the problems in the detection of enteroviruses in sewage.

Specimens were collected for examination by the immersion of water-sampling bottles (capacity 4 to 6 oz. [114 to 170 ml.]) in flowing sewage. After re-suspension of the deposited matter aliquots were centrifuged at 4,000 to 5,000 r.p.m. for one hour in a refrigerated centrifuge. The supernatant was inoculated into monkey kidney-tissue cultures without further treatment and also after centrifugation at 39,000 r.p.m. for 2½ hours with re-suspension of the sedimented pellet. Virus was isolated from 29 out of 56 specimens, in 17 instances by both methods, in 11 by ultracentrifugation only, and in one by standard centrifugation alone. Mixtures of virus types were infrequent. Little advantage was gained by using the method of plaque culture in preference to the purification by terminal dilution and blocking with homologous antiserum. Although many different serological types of enterovirus were demonstrated in the sewage from various districts, they included most of the types isolated from cases of poliomyelitis in human beings occurring during that period. As has been shown before, poliomyelitis viruses were isolated from sewage in the absence of overt cases of the disease.

J. E. M. Whitehead

1528. The Epidemiology of Tuberculosis

C. W. Ochs. Journal of the American Medical Association [J. Amer. med. Ass.] 179, 247-252, Jan. 27, 1962. 3 figs., 5 refs.

In 1959 an outbreak of pulmonary tuberculosis occurred aboard a destroyer of the United States Navy. In that year the incidence in the U.S. Navy of tuberculosis in subjects who had not had tuberculosis before was 52 per 100,000, and this outbreak afforded a rare opportunity to study the epidemiology of the disease in a closed and medically controlled community. Serial tuberculin tests and x-ray examinations were carried out in following the course of the outbreak. During an 18-month period 62 of the 236 officers and men were infected as evidenced by tuberculin conversion, and in 4 active lung lesions developed. A total of 30 men were admitted to hospital for investigation and treatment.

The 4 cases of pulmonary disease and the initial cases of tuberculin conversion could be explained on the basis of direct droplet infection, but many of the subsequent instances of tuberculin conversion occurred as long as 3 months after the last infectious patient had been removed from the ship, suggesting that re-suspended infective aerosols played an important part in the dissemination of the disease. An extensive programme of decontamination of the ship was put in hand and no further cases of tuberculin conversion were observed during the final survey carried out 6 months after the removal of the last active case.

[This is an interesting report.]

A. J. Karlish

1529. Detection of Tuberculosis in New York

A. B. ROBINS. Archives of Environmental Health [Arch. environm. Hlth] 4, 146-150, Feb., 1962.

INDUSTRIAL MEDICINE

1530. The Pharmacological Activity of Extracts of Cotton Dust

A. DAVENPORT and W. D. M. PATON. British Journal of Industrial Medicine [Brit. J. industr. Med.] 19, 19-32, Jan., 1962. 12 figs., 24 refs.

Aqueous extracts prepared from dust collected in the card-rooms of several cotton mills were found to contain some substance which contracted the smooth muscle of guinea-pig ileum, guinea-pig trachea, rat stomach, and rat duodenum. Chemical and pharmacological tests were carried out to try to identify the substance, which was shown to be dialysable, resistant to boiling for one hour, and not destroyed by the action of proteolytic enzymes. One of the samples contained histamine, but this could not be found in any of the other samples. However, all contained a small amount of 5-hydroxytryptamine. The particulate medium even after repeated washing was found to have some stimulant action on the guinea-pig ileum.

There appeared to be no reason at present to include a sensitization mechanism in the aetiology of byssinosis and there was no evidence for the release of histamine by the extracts in either cats or guinea-pigs, although a very small amount was released in rats. It is known that cotton dust extracts contain a pyrogen, but there was no evidence that this was responsible for the smooth muscle contractor properties. Jute dust is much less active than cotton dust and the activity differs qualitatively. The experiments with whole animals suggested that although smooth muscle contracting substances were present in the extracts, it is possible that the symptoms of byssinosis are caused by the release of some other active bronchoconstrictor substance in the tissues. The mechanism of the release is not known. It may be caused by a soluble principle in the extract or due to the presence of particulate matter in the dust. Kenneth M. A. Perry

1531. Some Pharmacological Actions of Cotton Dust and Other Vegetable Dusts

P. J. NICHOLLS. British Journal of Industrial Medicine [Brit. J. industr. Med.] 19, 33-41, Jan., 1962. 4 figs., 18 refs.

Aqueous extracts of cotton and other vegetable dusts cause contraction of the isolated ileum and tracheal muscle of the guinea-pig and of isolated human bronchial muscle. The levels of this contractor activity place the dusts of cotton, flax, and jute in this order, which reflects the liability of byssinosis occurring in the mills where these fibres are spun.

The present author, unlike Davenport and Paton [see Abstract 1530], found that extracts of cotton dust did possess a histamine-liberating activity and also contained, a component which increased permeability. The substances responsible for these actions are found in the pericarp and bracts of the cotton boll, and are therefore of plant origin. Histamine itself and 5-hydroxytryptamine were also found in some cotton dust samples. Histamine is not formed by bacterial action under the

conditions found in cotton mills. The substance responsible for contraction of smooth muscle is organic in origin, is heat-stable, and dialysable. Dusts from mills where byssinosis is known to occur all contain a smooth-muscle contractor substance. It is possible that on inhalation it gives rise to bronchoconstriction in man. As the active substance is water-soluble it probably acts locally in the lungs, but it could act systemically after absorption through the bronchial walls and it is possible that the permeability-increasing factor may cause bronchial oedema. The slow relaxation of bronchial muscle after contraction to dust and the oedema may explain the slow recovery of lung function observed in man after the inhalation of cotton dust. Kenneth M. A. Perry

1532. The Effect of Massive Doses of Riboflavine on the Development and Course of Experimental Silicosis in White Rats. (Влияние массивных доз витамина В2на развитие и течение экспериментального силикова у белых крыс)

M. I. RAZUMOV, B. K. SKIRKO, and A. JU. GRUBINA. *Apxus Патоловии* [Arh. Patol.] 23, 55-62, No. 8, 1961. 5 figs., 6 refs.

In the experiments here reported from the Institute of Nutrition, Moscow, riboflavine (vitamin B_2) was selected as being a known active agent in the tissue "redox" (reduction and oxidation) processes. In the authors' view, silicosis is the result of derangement of redox processes in the lungs induced by the rhythmical piezoelectrical impulses resulting from contact pressure on the lung tissues by the silica crystals during breathing. In rats crystalline silicon dioxide dust (particle size from 3 to 30 μ) was introduced through a tracheal puncture in quantities of 50 mg, in 0.5 ml, of saline. One of the four groups of rats (each of 5 animals) received 250 μ g, of riboflavine daily (a dose 10 times the normal daily requirement) throughout the experiment which lasted 10 months.

It was found that in the control group of rats receiving neither riboflavine nor dust the mean collagen content of dry lung tissue was 10%. In the group receiving riboflavine but no silica dust it was not significantly higher (12%), while in the group with experimentally induced silicosis but not given riboflavine it was 16%. However, in the riboflavine-treated group with induced silicosis the proportion of collagen was found to be as high as 25 to 30%. Thus riboflavine appears to aggravate silicosis. In the group of rats receiving riboflavine but not silica a lymphoid peribronchial hyperplasia developed.

A. Swan

1533. The Diffusion Chamber in Experimental Silicosis R. C. Curran and J. A. M. Ager. *Journal of Pathology and Bacteriology [J. Path. Bact.*] 83, 1-12, 1962. 22 figs., 30 refs.

Previous experiments with diffusion chambers demonstrated: (1) that "no toxic substances" were found about such chambers when full of silica dust even though the dust dissolved at much the same rate as it does when free in the tissues, and (2) that silica dust appeared to exert no specific stimulating effect on fibroblasts sur-

rounding the chamber or growing within it. The investigation reported in this paper from St. Thomas's Hospital, London, was therefore designed to test the effect on phagocytes of intimate contact with silica dust.

The chambers consisted of flat perspex rings with an internal diameter of 12 mm. closed on either side by porous membranes. Different pore sizes were used and ranged from $0.1~\mu$ to $5~\mu$. Some of the membranes were designed with "flap" valves, which did not allow dust to escape but permitted the entry of cells, capillaries, and fibrous tissue. The dust used was trydimite in some chambers and diamond in others. Most of the chambers were implanted in the peritoneal cavities of rets and removed at varying periods up to 28 days. After removal they were fixed, sectioned, and stained by various techniques.

Membranes with coarser pores (0.65 μ or larger) precipitated a more vigorous inflammatory reaction and omental adherence than the others, and the evidence pointed to this being due to some inflammatory agent released from polymorphonuclear leucocytes, many of which died within the pores. A dense fibrous capsule formed round the membranes. If tissue invading valvular chambers was avascular the silica dust within had no effect upon it, but when it contained capillary blood vessels silica caused "greatly increased fibrogenesis", and it appeared that something more than fibroblasts was required for silica to reveal its characteristic qualities. The authors suggest from the results of the expériments that "this effect of silica was largely mediated through its ability to kill phagocytes and thereby release a permeability factor".

[This is an interesting paper which should be read in the original.] W. Raymond Parkes

1534. Byssinosis: the Acute Effect on Ventilatory Capacity of Dusts in Cotton Ginneries, Cotton, Sisal, and Jute Mills

J. C. GILSON, H. STOTT, B. E. C. HOPWOOD, S. A. ROACH, C. B. McKerrow, and R. S. F. Schilling. British Journal of Industrial Medicine [Brit. J. undustr. Med.] 19, 9-18, Jan., 1962. 3 figs., 20 refs.

This paper gives an account of the changes in the indirect maximum breathing capacity of small groups of men working in and out of dust in a Uganda cotton mill, 3 cotton ginneries in Uganda, and 2 sisal factories in Kenya; the average age of the workers was between 23 and 29. Similar studies were also made in a jute mill in England when 20 subjects were investigated.

These studies showed that the ventilatory capacity of the workers was affected by the dust in the cotton mill and in the more dusty cotton ginnery but not in the less dusty ginneries. No significant effect was detected in the sisal factories or in the jute mill, despite much higher dust concentrations than in the cotton mill. Dust sampling divided the dust into three sizes: coarse (greater than 2 mm.), medium (between 7μ and 2 mm.), and fine (less than 7μ), and these samples were analysed for protein, ash, and cellulose. The fine and medium sisal and jute dusts contained between 9 and 19 mg. of protein per 100 cubic metres, whereas the cotton dusts contained 21 to

26 mg. per 100 cubic metres, which is significantly higher. The physiological changes observed in the employees in the cotton mill indicate the need for general dust measurement and control even when new grading machinery is installed in a new mill.

Kenneth M. A. Perry

1535. Influence of Emanations Produced by the Manipulation of Ethoxyline Resins on the Respiratory Tract. (Influence des émanations provenant des manipulations de résines éthoxylines sur les voies respiratoires)

J. M. Petit, J. Troquet, and J. Melon. Archives des maladies professionnelles, de médecine du travail et de sécurité sociale [Arch. Mal. prof.] 22, 718-725, Dec., 1961. 2 figs., 13 refs.

Ethoxyline resins have increasing application in the manufacture of electrical equipment. Their condensation products are obtained by the combination of the resin and a hardener, sometimes heated up to 120° C. They are irritants of skin and mucous membranes and some are potent skin allergens. Many workers in Belgium who mix these resins have complained of respiratory irritation and difficulty in breathing, chiefly during the heating of the resin-hardener mixtures. In order to estimate the possible psychological basis of these complaints and to minimize the necessity for individual cooperation, an investigation was carried out on 9 of these workers and also on one who had not been exposed to the resins but who suffered from an allergic rhinobronchitis.

The method used for estimating pulmonary resistance was that of interrupted inhalation of the air containing the fumes. Clinical and radiological tests and otorhino-laryngological examinations were also made and results were verified by control laboratory estimations. The two resin mixtures investigated were "araldite B" (solid, with a phthalic anhydride hardener) and "araldite F" (liquid, with a mixture of phthalic anhydride and hydrated phthalic acid). Pulmonary resistance was estimated by determining the relation between the flow of air, measured by a pneumotachograph, and the pressure gradient (the difference between the endo-alveolar and the buccal pressure) produced by interruptions, 2 per second for 150 milliseconds, of the air flow by means of closure of a tap.

The results of these estimations for analdite B were not statistically significant; but for analdite F they indicated some increase in resistance, and the fumes provoked some subjective irritation and a tendency to cough. In one subject, the non-exposed sufferer from an allergic disorder, the registered increase of pressure lasted longer and was accompanied by some asthmatic-like oppression. No clinical or radiological abnormalities were observed. or any lesions of the nasal, buccal, laryngeal, or tracheal mucous membranes. It was noted that even those workers showing skin reactions had no specific respiratory manifestations, indicating that these substances act as simple non-specific irritants of the upper respiratory passages rather than as allergens. The more marked effect of araldite F was attributed to the fact that while the vapour of analdite B condenses rapidly in the atmosphere with the formation of solid particles which are

probably deposited on the walls of the upper respiratory organs and do not reach the lower parts of the tract, the more stable araldite F can exert its irritant effect more readily on this lower region. Although this irritation is slight and benign, repeated contact might cause permanent lesions of the mucous membranes. It is suggested that this should be prevented by the installation of closed circuits, efficient local ventilation, and prohibition of employment of persons showing signs of nasal and bronchitic allergy or a tendency to hypersensitivity of the respiratory tract.

Ethel Browning

1536. Digestive and Respiratory Disorders Due to the Use of Epoxy Resins (Arabite). (Troubles digestifs et respiratoires lors de l'utilisation des résines epoxyliques (araldite))

M. OLTRAMARE. Revue lyonnaise de médecine [Rev. lyon. Méd.] 10, 1185-1192, Dec. 15, 1961 [received Feb., 1962]. 11 refs.

The main industrial hazard pertaining to the epoxy resins is their effect upon the skin, but as this has been fully documented elsewhere the present paper is limited to the digestive and respiratory disorders. First considered are those associated with the use of resins hardened with phthalic anhydride, the method of which is described in detail. A table shows the association between the separate processes in the preparation of "araldite" and the pathological effects encountered, these being conjunctivitis, rhinitis, cough, and bronchitis.

In the present study workers employed in the early stages of production (mixing, pouring, and demoulding) were most often affected, and here the concentration of phthalic anhydride in the working atmosphere was found to be greatest, amounting to 15 to 40 mg. per c. metre where mixing and pouring were carried out and to 8 mg. per c. metre in the demoulding area. A second table gives details of 4 cases of asthma in workers employed in the demoulding process. In only one of these 4 was there any other sign of allergy-an eczema which appeared after starting work on araldite. Asthma developed after a latent period of 5 to 6 months and was accompanied by anorexia, loss of weight, cough, dyspnoea' at night, with diminution of vital capacity and expiratory volume. Patch tests, both for the resin and the phthalic anhydride, were negative in the one case so, investigated. Eosinophilia was not present, but many eosinophil leucocytes were found in the sputum. On removal from contact with araldite recovery was rapid, all signs of irritation of the conjunctivae and respiratory tract disappearing in one or 2 weeks. In one of these men who later resumed his former work and another who was given work involving much lighter exposure to araldite the asthma reappeared. A third man who was less severely affected was able to continue at work without interruption and in his case the signs of bronchial irritation gradually subsided. It is suggested that these findings point to individual sensitivity rather than to a general allergic property in the chemical. Phthalic anhydride is scarcely soluble in water and sublimates directly from vapour to crystal, forming fine needles 1

to 2μ in diameter. Probably the irritative cough evoked by inhalation of very low concentration of the vapour is due to the mechanical irritation of these needle-like crystals. On the other hand, the associated conjunctivitis and tracheobronchitis are largely chemical in origin, for phthalic acid is produced on hydrolysis of the anhydride and this is a fairly strong acid, a saturated solution having a pH of 2. Since workers have been affected by exposure to an atmospheric concentration of phthalic anhydride of 8 mg. per c. metre, it is urged that the maximum allowable concentration (M.A.C.) should be below this figure.

The author then describes the respiratory and digestive disorders in workers using amine-hardened resins, for which the hardener employed was triethylene tetramine, , processed at normal bench temperature. Details of 3 cases are given in tabular form. There was no antecedent history of allergy. After several weeks at work and generally after 2 or 3 days of intense exposure to araldite, the symptoms developed simultaneously in the form of irritation of the conjunctivae and the upper respiratory tract, with accompanying gastro-intestinal disturbance manifested by nausea, vomiting, diarrhoea, and a sensation of burning and constriction in the epigastrium; in severe cases headache, vertigo, and ataxic gait also occurred. On removal from exposure the respiratory effects resolved within 10 to 15 days, but the gastric symptoms lasted much longer, continuing for over 5 months in one case. A barium meal showed the gastric mucosa to be hypertrophied and hypersecretory. One man who was only slightly affected suffered a swiftrelapse on return to his former work. The hardener, the amine, was held responsible. A further case is described in detail, that of a man who worked with a combination of glass fibre and araldite, used in alternate layers, the hardener being triethylene tetramine or an analogous polyamine. After 2 years at this work he developed first an eczema, then cough, conjunctivitis, asthma; eosinophilia, and an erythrocyte sedimentation rate of 14 mm. in one hour and 41 mm. in 2 hours [method not stated]. His condition remained stationary over one year, with emphysema and chronic bronchitis of, asthmatic type.

In conclusion emphasis is laid on the inhalation risk accompanying work with epoxy resin. The ideal protection is an enclosed system of production; second best would be the installation of adequate dust extraction equipment, with the use of dust masks alone as a last resort.

M. A. Dobbin Crawford

1537. Occupational Duodenal Ulcer Due to Carbon Tetrachloride. (Ulceres duodénaux professionnels par tétrachlorure de carbone)

C. GUERDJIKOFF. Revue lyonnaise de médecine [Rev. lyon. Méd.] 10, 1173-1184, Dec. 15, 1961 [received Feb., 1962]. 34 refs.

Attention is directed to the often quite different effects of acute and chronic intoxication with the chlorinated aliphatic hydrocarbons, these depending on the degree and duration of exposure to their vapour. If the LD 50 is taken as the measure of acute toxicity and the maxi-

mum allowable concentration (M.A.C.) as the guide to chronic toxicity it is found, for example, that toluene is a more potent acute narcotic than benzene, but benzene is far more dangerous in its long-term effect upon the blood-forming tissues; or again, trichlorethylene is a more potent narcotic than carbon tetrachloride, but the latter is far more toxic to the liver. In acute intoxication there is a rapid narcotic effect on the cerebral cortex. since it is easily reached and well supplied with blood. Subacute intoxication follows where exposure is inadequate to produce narcosis (except for a mild degree of giddiness, headache, nausea, and fatigue) but is too severe to be endured for long. At this level of intoxication it is the liver which suffers injury, in the form of degeneration of the centrilubular cells; the peripheral cells are less affected and show a remarkable power of regeneration.

In chronic intoxication, that is, where the M.A.C. is only slightly exceeded in the working atmosphere, it is now those tissues with a comparatively poor blood supply which are affected; the central nervous system does not respond to these small doses by narcosis, but it is injured by a grave disturbance of the enzymatic processes, the basal ganglia of the brain developing neurovegetative disturbances from the daily dose of poison. Damage to the kidney is probably secondary to metabolic derangements in the liver. In acute toxicity, therefore, these hydrocarbons can be placed in the following descending order of toxicity: tetrachlorethane, chloroform, tetrachlorethylene, trichlorethylene and dichlorethane, and lastly carbon tetrachloride. However, in subacute and chronic toxicity this order (with M.A.C. in p.p.m. in parentheses) becomes tetrachlorethane (5), carbon tetrachloride (25), chloroform (50), dichlorethane (100), and trichlorethylene and tetrachlorethylene

The author then stresses that in chronic intoxication with carbon tetrachloride it is remarkable how often severe gastro-intestinal symptoms are present, whereas the results of liver function tests are frequently within the normal range. Eight such cases are quoted and 5 of them are described in detail. The effects follow the pattern produced by all materials (such as the organic solvents, carbon monoxide, the soluble cyanides, and some of the metals) which attack the base of the brain, notablythe hypothalamus. In the case of carbon tetrachloride intoxication, however, the gastro-intestinal disorders are much greater than usual. They include progressive anorexia, with nausea and vomiting becoming more severe and frequent, and discomfort in the epigastrium which rapidly assumes the classic signs of duodenal ulcer; of the latter there was radiological confirmation in 2 of the 6 cases examined. In these patients the digestive history was not abnormal, and recovery soon followed withdrawal from exposure to the toxic vapour. It is emphasized that the toxicity of carbon tetrachloride is often underrated because its narcotic action is mild and liver damage follows only severe exposure, while the danger of chronic involvement of the hypothalamus is overlooked, although this may result in duodenal ulceration, severe haemorrhage, and perforation of the gut. M. A. Dobbin Crawford

Anaesthetics

1538. The Scope of Surface Cooling: an Experimental Study Using Quinidine as a Prophylactic against Ventricular Fibrillation

T. T. Currie, N. M. Cass, and J. D. Hicks. *Anaesthesia* [Anaesthesia] 17, 46-57, Jan., 1962. 10 refs.

An investigation was carried out at the Royal Melbourne Hospital, Australia, to determine whether reduction in the incidence of ventricular fibrillation during hypothermia produced by surface cooling would increase the usefulness of this hypothermic technique. Mongrel dogs were anaesthetized (without premedication) with intravenous thiopentone, gallamine, and atropine plus nitrous oxide and oxygen. The respirations were controlled, with carbon dioxide absorption.

The first two groups of dogs were given glucose and insulin before cooling and quinidine in a dose of 250 mg. regardless of body size. The first group (16 dogs) were cooled to 15° C., and in this group there were only 2 instances of ventricular fibrillation but there was a high incidence of asystole. The second group of 10 dogs were cooled to 20° C.; there was one instance of ventricular fibrillation and one late death. A third group of 14 dogs were cooled to 20° C. without glucose, insulin, or quinidine. Ventricular fibrillation occurred in 5 dogs. during cooling in 3 and early in rewarming in 2. The fourth group of 15 dogs were given 20 mg. of quinidine per kg. body weight intravenously as cooling to 20° C. began; all 15 dogs survived. Histological studies demonstrated infarction occasionally in dogs cooled to lower temperatures. Mark Swerdlow

1539. The Influence of Afferent Block in Hyperventilation Anaesthesia

J. D. KINNELL. Anaesthesia [Anaesthesia] 17, 58-63, Jan., 1962. 3 figs., 18 refs.

An investigation into the effect of afferent block on the electroencephalogram (EEG) in hyperventilation anaesthesia was carried out at the General Infirmary at Leeds on healthy patients undergoing routine surgery who were premedicated with pethidine and atropine, phenergan being occasionally used. Anaesthesia was usually induced with nitrous oxide and oxygen, but a small dose of thiopentone was given to some powerfully built men. p-Tubocurarine or gallamine was then administered, the patient intubated, and anaesthesia maintained with nitrous oxide (80%) and oxygen using a circle absorption system and hyperventilation at the rate of 25 to 30 litres per minute. EEG recordings were made throughout anaesthesia and surgery.

It was found that the theta rhythm (which appeared when the patient lost consciousness) slowed to a delta rhythm after 5 to 10 minutes of hyperventilation. The delta rhythm remained stable until the patient was stimulated, when it speeded up and reverted to theta rhythm. Delta activity was best maintained in lightly built subjects and in those undergoing operations not

involving peritoneal traction. When analgesia was supplemented by a lumbar epidural block hyperventilation readily produced delta waves, which were well maintained throughout surgery. If, however, stimulation was applied outside the area of the epidural block there was a temporary reversion to theta rhythm.

Mark Swerdlow

1540. The Duration of Inspiration during Artificial Ventilation of the Lungs

A. R. HUNTER. Anaesthesia [Anaesthesia] 17, 3-11, Jan., 1962. 6 figs., 12 refs.

The effect of altering the durations of inspiration and expiration on the tidal volume during artificial ventilation of the lungs was studied in anaesthetised patients fat the Royal Infirmary and Baguley Hospital, Manchester]. When a Blease P6 apparatus was used for this purpose, prolongation of inspiration caused a very considerable increase in tidal volume. This was not, however, sufficient to compensate for the reduction in alveolar ventilation consequent upon the reduction of rate, if the inspiration: expiration ratio was to remain at 1:2. A similar increase in tidal volume with prolongation of inspiration was observed during one lung anaesthesia conducted with the aid of a Carlens tube. Alteration in the duration of expiration produced only slight changes in tidal volume. When inspiration was reduced to less than one second or expiration to less than two seconds the tidal volume fell off fairly sharply. There was, therefore, nothing to be gained by increasing the . rate of a respirator, with characteristics similar to those of the Blease P6, to more than 20 per minute.-[From the author's summary.1

1541. L 67—Experimental Evaluation of a New Local Anaesthetic in Man. [In English]

E. ERIKSSON. Acta anaesthesiologica Scandinavica [Acta anaesth. scand.] 5, 191-205, 1961. 2 figs., 12 refs.

L 67 — α -n-propylamino-s-methylpropionanilide — a new local anaesthetic, was compared with "xylocaine" [lignocaine] in a series of experimental tests on human beings. Intracutaneous wheals, finger nerve blocks, caudal blocks and spinal blocks were induced, L 67 having a somewhat better anaesthetic effect mainly by virtue of a longer duration of action. No differences in latency were found. L 67 had no demonstrable side effects.

Finger nerve blocks were specially investigated in order to establish the influence of age on the duration of anaesthesia. The role of intact circulation in the duration of anaesthesia produced by intracutaneous administration was also studied. A discussion is presented on the degree to which the observed differences between xylocaine and L 67 might be due to a direct action of the local anaesthetic upon the circulation in the anaesthetised region.—
[Author's summary.]

Radiology

1542. Criticality Accidents in Vinca, Yugoslavia, and Oak Ridge, Tennessee. Comparison of Radiation Injuries and Results of Therapy

G. A. Andrews. Journal of the American Medical Association [J. Amer. med. Ass.] 179, 191-197, Jan. 20, 1962. 4 figs., 12 refs.

In 1958 two major radiation accidents occurred, one at Oak Ridge, Tennessee, and one at Vinca, Yugoslavia, and in this paper from Oak Ridge Institute of Nuclear Studies the radiation injuries and their response to treatment are described.

The radiation consisted of neutrons and gamma rays of different energies. It was estimated that the 5 workers at Oak Ridge received a total body dose of 236 to 365 rads, this estimation being based on radioactivesodium measurements on burros exposed to comparable conditions. The 6 Yugoslav workers probably received total body doses ranging from 207 to 436 rads. All the patients except one in each group had nausea and vomiting. The Yugoslav receiving the highest dose also had diarrhoea, insomnia, and headache. Erythema, weakness, and conjunctivitis were common in the Yugoslavs but not in the Americans, and epilation was more severe in the former. The Oak Ridge patients received minimal treatment, while the Vinca patients received blood and platelet transfusions, antibiotics, and dietary supplements, and in 5 of the 6, bone-marrow transfusions also.

The most heavily exposed Yugoslav patient died 4 weeks after exposure. Initially in this case pancytopenia, intussusception, lower-nephron nephrosis, jaundice, and haemorrhages developed. Post-mortem examination revealed severe radiation damage to many organs. The bone-marrow depression which occurred in all the patients is described. It is considered that the bone-marrow transfusions given to the Yugoslavs did produce a temporary functioning graft, but it was given rather late (after 28 to 36 days) and therefore did not appreciably affect the haematological recovery that was taking place.

M. Sutton

1543. Mammography of Breast Sarcoma

S. M. BERGER and J. GERSHON-COHEN. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 87, 76-81, Jan., 1962. 7 figs., 9 refs.

Sarcoma of the breast is a rare lesion. The roentgenographic appearance of sarcoma is that of a large, dense, rapidly growing, well-defined mass. It is not infiltrative and tends to resemble benign lesions such as cysts' and fibroadenomata. The history of rapid growth should put the roentgenologist on guard and lead him to urge a diagnostic resection, even though the lesion may resemble a benign process on the roentgenogram.— [Authors' summary.] 1544. Diagnostic Pneumomediastinum

D. L. Hughes, W. Hanafee, and B. J. O'Loughlin. Radiology [Radiology] 78, 12-18, Jan., 1962. 12 figs.

The authors of this paper from the University of California Medical Center, Los Angeles, describe two methods of direct diagnostic pneumomediastinum, with reference to 12 cases investigated for various conditions. The first method is the sternal notch approach. With the patient supine and the neck extended a 20-gauge spinal needle, bent at an angle of 120 degrees approximately 2 cm. from its tip, is introduced after local anaesthesia so that the tip lies not more than 1 cm. posterior to the centre of the manubrium. After checking that a vessel has not been entered, an additional 1 to 2 ml. of anaesthetic is injected to spread apart the tissue at the needle tip. An average of 400 to 500 ml. of oxygen is slowly introduced over about 5 minutes. Little discomfort is experienced. After the needle is removed the patient is placed prone for 5 to 10 minutes. Anteroposterior and lateral laminagraphy is then performed. An alternative and equally satisfactory approach is the subxiphoid route. which is preferable in patients with anterior superior mediastinal masses. The needle is inserted near the tip of the xiphoid, so that the point comes to lie immediately behind it. In the authors' view these methods are more certain to give good results than presacral air insufflation. They point out that Italian workers have used pneumomediastinum to demonstrate and differentiate mediastinal space-occupying lesions. The technique is considered to be simple and safe.

B. Golberg

1545. Valves of the Common Carotid Artery during Angiography

W. E. GANNON. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 86, 1050-1057, Dec., 1961. 12 figs., 6 refs.

The author of this paper from the State University of New York Downstate Medical Center, Brooklyn, describes 4 cases of artificial valve formation in the common carotid artery. The valve is formed during carotid angiography by needle puncture of the intima of the posterior wall of the vessel causing a laceration which enables the intima to be elevated and dissected from the media by the pressure of the blood flow, thus forming a valve. This valve causes partial obstruction to blood flow under normal conditions, and under the increased pressure occurring during injection of the contrast medium the obstruction becomes almost complete.

Radiologically there is a complete or almost complete block in the common carotid artery in the form of a meniscus with the concavity inferiorly. This lasts for several seconds and then the contrast material starts to escape around the valve and there is usually faint visualization of the region of the bifurcation and the RADIOLOGY

proximal part of the internal and external carotid arteries. A faint crescentic line may be seen either above or below the point of the needle representing the free edge of the elevated intima.

The lesion is important because it may lead to an erroneous diagnosis of common carotid occlusion. It may, of course, give rise to dissecting haematoma and thrombosis, but the latter complications appear to be comparatively rare. The author suggests that if a valve is suspected a second puncture may be made higher up in the common carotid artery or in the internal carotid artery. Other procedures which may help in the diagnosis of this iatrogenic condition are measurement of the retinal arterial pressures or compression of the contralateral common carotid artery.

A review of 1,224 angiograms revealed only 3 cases of valve formation, an incidence of approximately 0.25%. However, abnormal signs or symptoms following carotid artery puncture are rare and it may be that intimal damage without actual valve formation is much commoner than this.

Arnold Appleby

1546. Phlebography in the Detection of Deep-seated Lymphadenopathy. Its Diagnostic and Therapeutic Value in Malignant Blood Diseases. (La phlébographie dans le dépistage des adénopathies profondes. Son intérêt diagnostique et thérapeutique dans les hémopathies malignes)

G. MARCHAL, J. BERNARD, N. ARVAY, G. BILSKI-PASQUIER, J. ECOIFFIER, and J. D. PICARD. *Presse médicale [Presse méd.]* 69, 2586–2588, Dec. 25, 1961. 11 figs., 10 refs.

The realization of the ease with which veins are compressed and deviated by adjoining masses of enlarged lymph nodes stimulated the authors to study the results of phlebography of the inferior vena cava in various malignant blood diseases. This was carried out by simultaneous catheterization of both femoral veins and injection into them of a large quantity (80 ml.) of opaque medium. A serial device capable of exposing 10 films in 10 seconds was found to be essential. Normally the inferior vena cava should fill completely and no reflux should occur into its collaterals; however, a little reflux may occur normally for 2 to 3 cm. up the hypogastric veins.

The left border of the inferior vena cava is less distinct at the level where the left common iliac vein is crossed by the corresponding artery, and there is a defect at the level of the 12th dorsal vertebra due to the influx of subhepatic venous blood. The inferior vena cava is displaced to the right and separated from the aorta by enlarged lymph nodes; obstruction is well shown by reflux into the hypogastric and renal veins. The examination enables enlarged nodes in the lumbar region to be accurately located so that they can be efficiently treated by radiotherapy; their progress under treatment can also be demonstrated. The method should be used when intravenous pyelography and barium visualization of the duodenal loop have failed to give information. The technique is described and illustrated.

John H. L. Conway-Hughes

1547. Non-specific Changes in the Terminal Ileum in Infants. (Unspezifische Veränderungen am terminalen Ileum beim Kinde)

M. A. LASSRICH. Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin [Fortschr. Röntgenstr.] 95, 757-764, Dec., 1961. 13 figs., 21 refs.

In most children lymphatic nodes in the terminal ileum are plentiful and may cause a polypoid pattern of varying extent on x-ray examination. When these nodes are seen to undergo changes these do not always run parallel to other lymphatic hypertrophies, such as those of the tonsils or adenoids, and usually reach their maximum at the age of about 5 or 6 years. Such changes by themselves are not pathological. If, however, there is also thickening of the terminal ileum, possibly with loss of contractility, and tenderness and swelling of the ileo-caecal valve, then the changes have pathological significance and correspond to Golden's non-sclerosing ileitis.

F. M. Abeles

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1548. The X-ray Diagnosis of Meckel's Diverticulum. (Die Röntgendiagnostic des Meckelschen Divertikels) W. Wenz. Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin [Fortschr. Röntgenstr.] 95, 782-792, Dec., 1961. 13 figs., bibliography.

The radiographic diagnosis of Meckel's diverticulum has often proved unsuccessful in the past, and for this there are several reasons: (1) the wall is contractile and cannot therefore be expected to remain filled; (2) inflammatory changes may occlude an already narrow entrance; (3) gastric mucosa, if present, is most frequently seen at the entrance to the diverticulum and it is here that peptic ulceration occurs and leads to occlusion: (4) if the diverticulum, with its fibrous band pointing towards the umbilicus, leads to volvulus or intussusception then its entrance is generally kinked and blocked. In spite of these difficulties the condition is frequently diagnosable. The author advises that in performing follow-through barium studies accelerators should not be used. F. M. Abeles

1549. The Radiologic Findings in Histologically Verified Atrophic Gastritis and Gastric Atrophy

R. A. Joske and B. F. Vaughan. Gastroenterology [Gastroenterology] 42, 7-15, Jan., 1962. 11 figs., 17 refs.

A comparative study of the histology of gastric biopsy specimens and the radiological appearances of the stomach in 160 patients with gastro-intestinal or haematological symptoms is reported from the Royal Perth Hospital and the University of Western Australia, Perth. The biopsy findings were classified in five grades of increasingly severe mucosal change. The radiographs were obtained in three projections: (1) supine with the gastric mucosa coated with 65 ml. of barium sulphate suspension; (2) erect after a further 300 ml. of barium; and (3) supine after a total of 500 ml. of suspension. A radiological diagnosis of gastric atrophy was based, according to the criteria of Laws and Pitman (Brit. J. Radiol., 1960, 23, 229), on: (1) a long tubular stomach with an absence of rugal markings on the greater curva-

ture; (2) a small fundal dome and absent rugae ("bald fundus"); and (3) thin, fine, gastric folds—"tissue-paper folds"—in the fundus or body of the stomach. Two other characteristic changes were added: (4) marked hypotonia, so that the narrow fundus became distended in the supine position—the "H-bomb sign"; and (5) disappearance of the mucosal pattern, clearly seen with a little barium, as the stomach distended.

Of 100 patients without focal gastric lesions, gastric atrophy was diagnosed radiologically in 37. Good general agreement was obtained between the histological and radiological findings. Of 60 patients with focal gastric or duodenal lesions, gastric atrophy was diagnosed radiologically in only 10 (17% compared with 37%), but the frequency of severe histological changes was approximately the same, so that all degrees of histological abnormality occurred without corresponding radiological change. It is considered possible that this discrepancy is due to zonal gastritis occurring in relation to the focal lesion, Radiological evidence of gastric atrophy was strikingly frequent in patients who had undergone partial gastrectomy, and was not related to the initial pathology or to other clinical or laboratory. data analysed. B. Golberg

1550. Isotope Nephrography as a Diagnostic Method for Use in Radiotherapy. (Die Isotopen-Nephrographie als diagnostische Methode für den Strahlentherapeuten) K. ZUM WINKEL, J. BECKER, and K. E. SCHEER. Strahlentherapie [Strahlentherapie] 116, 489-501, Dec., 1961. 6 figs., 46 refs.

The authors report from the University of Heidelberg that in patients with abdominal tumours, in order to assess any renal damage which may be present due either to the malignancy itself or to subsequent radiotherapy, the most informative method is injection of "hippuran" (sodium iodohippurate) containing radioactive iodine. Hippuran has the advantage of being excreted exclusively by the kidneys. Four scintillation counters are applied, 2 being over the kidneys, one over the bladder, and one over the heart; the results are recorded on magnetic tape.

The curves obtained show three phases: (1) increasing blood flow to the kidneys; (2) phase of tubular secretion; and (3) drainage of the outflow system. For collimation, cylinders with an aperture of 4 cm. and a height of 5 cm. are best. The authors state that damage to the renal parenchyma appears to be less with the cobalt bomb and supervoltage therapy than with the more conventional methods of radiotherapy. (Observations covering longer post-radiation periods are to be published later.)

1551. Laminagraphy, an Aid in Accurate Localization in Congenital Hip Dysplasia

W. S. ALTMAN and V. MORACE. Radiology [Radiology] 78, 19-28, Jan., 1962. 6 figs., 3 refs.

For accurate location in congenital hip dysplasia the authors of this paper from Quincy City Hospital, Massachusetts, and the University of Naples, Italy, havefound multisection laminagraphy ("book laminagraphy") to be the procedure of choice. Three cuts were used—the centre one at the level of the normal hip, a second cut 1 cm. posterior to the normal hip, and a third 1 cm. anterior to the normal—satisfactory views being obtained even through plaster casts. Repeat radiographs were seldom necessary. The gonadal dosewas less than that received in tube-shift studies or from radiographs taken in two planes, being "reduced by a factor ranging from 80.7 to 84.7%".

The majority of hip dislocations were found to be lateral or lateral and cephalad, the normal hip being used for comparison. Anterior dislocations occurred only with trauma or after attempted reduction, while posterior dislocations were usually found in older untreated children. Cases of bilateral dislocation were more difficult to diagnose. The authors state that in their experience if the upper portion of the Y cartilage and the "tear-drop" of the acetabulum are well demonstrated the normal plane of the hip-joint is in focus. If the abnormal femoral head is in focus with the puboischial ramus, the head is too far posterior; if the abnormal head is in focus with the pubic arch it is too far anterior. The most valuable information is obtained from post-reduction studies. B. Goiberg

. RADIOTHERAPY

1552. Results of Radiotherapy of Patients with Tumours of the Brain and Carchoma of the Oesophagus and Bronchus with the 31-MeV. Betatron (Photons) in Comparison with 200-kV. Radiotherapy. (Resultate der Strahlenbehandlung von Patienten mit Hirntumoren, Osophagus- und Bronchuskarzinom mit 31-MeV-Betatron (Photonen) im Vergleich zur 200-kV-Röntgenbestrahlung)

U. Cocchi. Strahlentherapie [Strahlentherapie] 117, 3-17, Jan., 1962. 5 figs.

This paper records the experience gained in the treatment of over 1,000 patients during the past 10 years at the University Radiotherapy Clinic, Zürich, with x rays from a 31-MeV betatron. The advantages of this supervoltage radiation include sparing of the skin (the maximum dose being received at a depth of 5 to 6 cm.), sharp definition of the beam, homogenous dosage distribution, and equalization of absorption in soft tissue and bone. Most of the patients had large and inoperable tumours and were in poor general condition. The usual daily tumour dose ranged from 165 to 200 rads, and total doses in most cases from 5,500 to 7,500 rads.

Among the 137 cases of intracranial tumour the results in glioblastoma multiforme and unclassifiable malignant glioma were very poor, and no better than with conventional deep x rays (200 kV.). Astrocytoma, however, showed better results; thus at 3 years 11 (61%) of 18 patients were alive and 9 (50%) were symptom-free, compared with 45% and 25% respectively of those treated with deep x rays. The results for oesophageal tumours were in general poor, but increased experience and better selection after 1955 made for better results; thus of 73 patients treated before 1956 there were no survivors at

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3 years, whereas after 1956 there were 2 3-year survivors cedure. If there is submucosal involvement palliative out of 13 patients (15 4%). Comparable figures for treatment only (dosage about 3,500 r.) should be aimed deep x rays were 12 out of 225 patients (5%). Among 200 cases of bronchial carcinoma, there was only a slight difference in average survival of patients with squamous lesions as compared with small-celled lesions. Postmortem examination showed that, with smaller growths, local eradication could be achieved with 6,000 rads and over, but with large growths there was no significant regression even after doses of 7,000 to 8,000 rads. Supervoltage gave only slight improvement in survival time (6 out of 114 (5%) compared with 6 out of 191 (3%) for 200 kV: at 3 years). The symptom-free figures, however, showed an advantage in favour of supervoltage [actual figures for 200-kV. x rays not given]. In 121 cases of tumour of the bladder there were again better results after 1955 (6 out of 36 (17%) symptom-free at 3, years, compared with 5% for the earlier period; [200kV. figures not given). Post-mortem findings showed complete local eradication. Tables showing results for the various sites, together with results year by year, are included in the paper. J. Walter

1553. Tracheo-bronchial Involvement in the Evolution of Oesophageal Cancer: Diagnostic Verification and Limits of Radiotherapy. (L'interessamento tracheo-bronchiale nella evoluzione del cancro esofageo: accertamento diagnostico e limiti della radioterapia) -

C. Jucker. Radiobiologia, radioterapia e fisica medica [Radiobiol. Radioter. Fis. med.] 16, 278-295, 1961. 7 figs., 9 refs.

Examination of 100 cases of cancer of the oesophagus at the Institut Gustave-Roussy, Villejuif, Seine, leads the author to emphasize the importance of routine examination of neighbouring structures by radiology and bronchoscopy. Lateral films may show encroachment on the tracheal lumen by the primary tumour or by secondaries in lymph nodes. Contrast media and tomography are also valuable. Even neoplastic lesions below the bifurcation may produce signs by upward extension or by secondary involvement of lymph nodes. Projection into the lumen of the trachea or left main bronchus is manifested by signs of compression, while actual invasion is shown by typical deformities of the lumen. by rigidity and fixity of the wall, by oedema of the mucosa with ready bleeding, or by visible infiltration. Among the author's 100 cases compression was found in 30 and invasion in 18. Compression may be due to the primary tumour, to dilatation of the oesophagus, or to secondary nodes, and radiography and oesophagoscopy will help to decide which. Mucosal invasion was found in 8 cases and confirmed by biopsy or examination of aspirated material.

The author points out that these findings are important in determining treatment. Respiratory-tract involvement rules out surgery, and also predisposes to the development of fistula after radiotherapy. Experience in several hundred cases at the Institut has shown that radical irradiation should be attempted only if there are no signs of involvement. If the respiratory mucosa is invaded, gastrostomy should be the sole palliative pro- J. Walter

1554. Long-term Results of Stereotaxic Irradiation with Isotopes of Tumours of the Hypophysis (Compared with Those of Open Transcranial Operation). (Langzeitergebnisse der stereotaktischen Radio-Isotopenbestrahlung von Hypophysentumoren (im Vergleich zur transkraniellen offenen Operation))

F. MUNDINGER. Strahlentherapie [Strahlentherapie] 116, 523-535, Dec., 1961. 9 figs., 35 refs.

The surgical treatment of pituitary tumours carries a high mortality, while radical external radiation may damage the mid-brain or optic nerves. At the University Neurosurgical Clinic, Freiburg-im-Breisgau, the method of implantation of radioactive sources has been developed, using a stereotaxic technique which provides an accuracy of ± 0.5 mm. Radioactive phosphorus was first used, but now radioactive gold, adsorbed on graphite particles, is preferred. A minimum particle size of 50 μ is necessary, as smaller particles lead to dangerous loss by diffusion. Implantation may be either the primary treatment or employed as a secondary measure to treat the residue following surgical removal of most of the tumour. A transfrontal approach is usually preferred to the trans-sphenoidal route.

The results at between 5 and 7 years for a series of 87 patients are presented and compared with a surgical series of 66 cases. The operative mortality was nil for the primary cases and one death (1.6%) for the secondary cases, but 19% for the surgical series. The late effects on vision and the visual fields are given in detail for chromophobe, eosinophil, and basophil adenomata and cranio-pharyngioma. In both respects the results after radiation, especially secondary radiation, were significantly better than after surgery. The 5-to 6-year survival rates were 90.4% for secondary radiation cases, 76.1% for primary radiation, and 62% for the surgery cases. Postoperative complications considered to be due to radiation effects included palsies of the 3rd and 4th cranial nerves, worsening of the chiasma syndrome, and disturbances of consciousness. Decompression was required in 6 cases after one to 30 days for the following reasons: suprasellar extension, cystic liquefaction, oedema of tumour, and epidural haematoma. Recurrences and late complications (up to 3 years) were seen in 10 cases, of which 5 came to operation, in one because of a large suprasellar tumour, while the other 4, had arachnoiditis of the optic chiasma with disturbancesof blood supply attributed to the gamma radiation.

The results have led the author to advocate a transcranial intradural surgical approach for cases with an advanced chiasma syndrome, followed after healing of the wound by secondary transfrontal stereotaxic implantation. If such cases are inoperable, primary trans-. sphenoidal implantation is advised, as also for most cases of eosinophil and basophil adenoma. For the others, primary transfrontal implantation should be considered. with surgery held in reserve in case of later recurrence or . complications. J. Walter

1555. Radiation Therapy of Pitultary Adenomas with Associated Visual Impairment

M. Y. COLBY JR. and T. P. KEARNS. Proceedings of the Staff Meetings of the Mayo Clinic [Proc. Mayo Clin.] 37, 15-24, Jan. 3, 1962. 4 figs.; 7 refs.

From the Mayo Clinic the authors report the results of radiotherapy in 127 cases of chromophobe adenoma of the pituitary gland and 22 cases of acromegaly, in all of which there was impairment of vision. Most of the patients were treated by a multiple small-dose method, receiving a tumour dose of 800 r. (200-kV. x rays) in 3 to 5 days, repeated once or twice at monthly intervals (though the authors' current method is to give a tumour dose of 3,500 r. in 3 weeks from a telecobalt unit). The technique of the American Medical Association was used for assessment of visual impairment before and after treatment.

It was found that at 2 years vision was improved in 45 (44%) of 102 of the patients with chromophobe adenoma and in 11 (73%) of 15 of those with acromegaly, while at 5 years there was improvement in 37% (33 out of 89) and 60% (9 out of 15) of these cases respectively. - Of the 89 patients with chromophobe adenoma followed for 5 years 22 received post-irradiation surgery because of failing vision, and in 9 of these vision subsequently improved. [The number of postoperative deaths is not stated.] It is pointed out that the hazards of radiotherapy are slight compared with those of surgery, only one out of the total of 149 patients dying within 2 weeks of completing treatment, and this patient died at home from a cause unknown. In addition to the 45 patients (36%) with chromophobe adenoma who had deficiency of anterior pituitary function when first seen, a further 20 (16%) developed such deficiency later. It is suggested that this was not related to the radiotherapy.

K. E. Halnan-

1556. Breast Cancer. Five Year Results: Two Random Series of Simple Mastectomy with Postoperative Irradiation versus Extended Radical Mastectomy

S. KAAE and H. JOHANSEN. American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine [Amer. J. Roentgenol.] 87, 82-88, Jan., 1962. 4 figs., 20 refs.

Since November, 1951, all new patients with breast cancer from Copenhagen admitted to the Radium Centre, have been divided into two groups. In one group the operable cases had simple mastectomy with post-operative roentgen irradiation by the McWhirter method. In the other group the operable cases had extended radical mastectomy by the method of Dahl-Iversen. The preliminary therapeutic results show no definite difference between the results of the two methods.—[Authors' summary.]

1557. Vesical Haemorrhage after Megavoltage Irradia-

D. P. B. TURNER British Medical Journal [Brit. med. J.] 2, 1462-1466, Dec. 2, 1961. 5 refs.

Out of a series of 17 cases of extensive vesical neoplasm treated by megavoltage irradiation there were 4 cases of persistent haemorrhage, the haemorrhage starting several

months after treatment. It appeared that this haemorrhage occurred from areas of residual or recurrent tumour. This complication after megavoltage irradiation is regarded as an extremely serious condition, and it is suggested that if conservative measures are not effective. within 2 to 3 weeks total cystectomy should be seriously considered, even if cystoscopy shows almost complete disappearance of the original tumour. In the author's experience cystoscopic diathermy did not prove practicable and ligation of the internal iliac arteries was ineffective. The haemorrhage, however, was usually controlled by transvesical diathermic excision of the bleeding area. The author states that this operation: alone, possibly repeated, may be expected to suffice in -some cases, while in others it may be a useful preliminary to total cystectomy, allowing the patient to recover fully from the loss of blood. J. D. Bradshaw

1558. Carcinoma of the Anus and Anal Canal I. G. WILLIAMS. Clinical Radiology [Clin. Radiol.] 13, 30–34, Jan., 1962. 9 refs.

In this communication from St. Bartholomew's Hospital, London, the author reviews the anatomy and pathology of carcinoma at the anal margin and within the anal canal. Surgery and radiotherapy are the two accepted methods of treatment, but there are no special features to indicate which should be the primary treatment. The likelihood of success and the reliability of each method have to be carefully assessed, taking into consideration the age and general condition of the patient together with the site, extent, and histological type of the tumour.

In the period 1938–58 37 patients (20 males) with cancer of the anal region have been treated by irradiation. All were unsuitable for surgery either because of the advanced stage of the disease or the general condition of the patients, whose average age was 65 years. Histologically the tumour was squamous-cell carcinoma in 32 cases (one-third of which were anaplastic), transitional-cell carcinoma in 2, and basal-cell carcinoma in 3. The incidence of lymph-node involvement was high and half the patients had either fixed or bilateral inguinal lymph-node metastases; in 3 cases involved pelvic nodes were found at laparotomy.

Radium needle implant is suitable for well differentiated tumours at the anal margin or low in the canal; a dose of 5,000 to 6,000 r. is given over 8 to 10 days. The 3 patients so treated are alive and free from recurrence at 2, 4, and 10 years respectively. For larger and anaplastic tumours external irradiation is advised, a tumour dose of about 5,000 r. being given, using x rays generated at 1 million volts (H.V.L. 10 mm. Cu). No case of radionecrosis has occurred in the last 10 years. Before this time patients received 4,500 r. in 28 days and 6 developed necrosis. Three patients also required a colostomy for anal fibrosis and stricture. Of 32 patients treated more than 5 years ago 12 (37.5%) are alive and . free of disease, while 2 others are well 2 and 3 years respectively after treatment. Of 7 long-term survivors 3 lived for over 10 years and 4 for over 6 years, 3 dying from causes other than carcinoma. W. Duncan

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